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MALARIA

AND

MALARIAL DISEASES

[illegible]

BY

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PRINTING AND BOOKBINDING COMPANY,
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L156
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PREFACE.

It was with considerable hesitation that the writer accepted the proposition of Messrs. Wm. Wood & Co. to prepare for them a volume upon "Malaria and Malarial Diseases" by a specified date (May 1, 1884). The time allotted to the task seemed short, in view of the extent of the subject and the dimensions of the required volume. Moreover, a portion of the time which the Publishers deemed sufficient would necessarily be consumed in the completion of other literary work already commenced, and it would be necessary to undertake a long and expensive journey for the purpose of consulting the literature of the subject in a properly equipped medical library; for the writer was stationed upon the Pacific Coast, and the medical library which he naturally looked upon as the source from which the required data—the recorded experience of physicians in all parts of the world—could best be obtained, was on the other side of the continent, in Washington. Under these circumstances, it would perhaps have been wise to have declined the undertaking. The task was a difficult one, and in view of the widely different opinions held by physicians in regard to the nature of malaria, and of the morbid phenomena which it may produce in man, there was little hope that it would be accomplished in a manner to give general satisfaction. But the subject is one in which the writer is deeply interested, and while he fully recognized that unsolved problems connected with it are not likely to be settled by the pen, it seemed a favorable opportunity to review the literature of the subject and to compare the recorded experience of recent foreign authors, whose works have not been republished in this country, with that of physicians in the malarious sections of the United States. If, then, it might have been wiser to decline the undertaking, the writer failed to exercise this amount of discretion, and now, after six months' continuous application, has before him the manuscript for the proposed volume, and with the date near at hand when this is to be delivered to the Publishers, seats himself at his desk to write a Preface, with the consciousness that more time, more labor, more ability, and a more ample experience would have enabled him to make a much better book, but convinced, nevertheless, that the present volume will be found to contain much valuable information not elsewhere accessible to American readers, and that the very considerable portion of the work printed in small type, at least, will be appreciated. Several of the authors most freely quoted—Colin, Morehead, Fayrer, and Bérenger Féraud—have had an extended experience in intensely malarious regions—Italy, India, Algeria, the West Coast of Africa, etc.—and are recognized as among the highest recent authorities upon the subject. By drawing largely upon their experience the writer trusts that he has succeeded to some extent in complying with the wishes of the Publishers, and in making a book which will be of "practical value to general practitioners."

FORT MASON, SAN FRANCISCO,
April 20, 1884.

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MALARIA

AND

MALARIAL DISEASES.

INTRODUCTION.

THE word malaria is used by some authors, in accordance with its etymology, as a general term to include all kinds of bad air, or at least of disease-producing bad air. Thus Dr. Herbert Barker, F.R.S., of Edinburgh, published a work in 1863, founded upon the Fothergillian Prize Essay of 1859, entitled "On Malaria and Miasmata and their Influence in the Production of Typhus and Typhoid Fevers, Cholera and the Exanthemata." In this work the author employs the term malaria in its widest signification. He defines a malarious agent as any agent which, being so diffused through the air as to admit of being inhaled, possesses the power of exciting specific symptoms in the person who inhales it.

Aitken also uses the word in a general sense, and in order to designate the special kind of malaria to which he has reference uses a qualifying word Thus he speaks of "paludal malarious poison" and of "animal malaria poison,"[1] of the malaria of yellow fever, etc.

But this use of the term is no longer justifiable, inasmuch as the highest authorities in medical literature and the profession generally have adopted this as the name of a special kind of poison, not necessarily aëriform, which produces certain well-defined morbid phenomena, viz., the periodic fevers.

Much confusion has arisen from this use of the word "malaria," both in a general and in a restricted sense, and also from the uncertainty which exists as to the etiology of certain forms of disease, which are often ascribed to malaria, but which do not exhibit well-marked periodicity and are not cured by the administration of quinine. Thus the writer was recently informed by the Secretary of the State Board of Health of one of the Eastern States, that in addition to intermittent, remittent, and typho-malarial fevers, a form of malarial disease prevails in his State which appears in his reports as "malarial fever." This fever has a duration of from three to four weeks, and cannot be abridged by the administration of quinine.

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[1] Science and Practice of Medicine, vol. i., p. 212.

The various types of intermittent and remittent fever which are cured by quinine are by common consent recognized as due to malarial poisoning, and while we admit that malarial fevers may sometimes assume a continuous course—usually, no doubt, as the result of a complication—we must insist that the prevalence of periodic fevers be taken as the test of the presence of malaria. In other words, where ordinary intermittent fever, which is the most common manifestation of malarial toxæmia, does not occur as an endemic disease, there we believe that malaria, properly so called, is not evolved from the soil. And if it can be shown that continued fevers not amenable to the action of quinine prevail in localities where paludal intermittents and remittents are unknown, then we are justified in assuming for them a different etiology from that of the last-named forms of disease. When we hear that in a certain city or section of country where intermittent fevers of local origin are extremely rare or unknown the inhabitants suffer greatly from "malaria," and when in such a city or region of country we find a considerable number of deaths ascribed to "malarial fevers," we take the liberty of doubting whether the fever in question is produced by the kind of malaria which is the special subject of consideration in the present volume.

This kind of malaria manifests its presence more commonly in rural districts than in cities. It shows far greater activity in the tropics than in northern latitudes, and during the winter months its evolution is, to a great extent, arrested in localities north of 40° north latitude. Moreover, we have a potent remedy against the effects of this poison, if not an antidote for the poison itself, and except in localities where conditions are extremely favorable for its production, death from malarial toxæmia is extremely rare. Even the congestive forms of intermittent and remittent fever, which presumably result from exposure to malaria in its most intense and concentrated form, are commonly cured by the timely and vigorous administration of quinine.

In support of our assertion that death from malarial fevers is a rare event in northern latitudes, we submit the statistics relating to malarial diseases at military stations in the "Division of the Atlantic," which includes the States of Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut, New York, New Jersey, Delaware, Maryland, Virginia, West Virginia, Ohio, Michigan, and Wisconsin. These statistics for four years—1870–74—are recorded in the "Report on Hygiene" (Surgeon General's Office, Washington, May 1, 1875). From this report we learn that at thirty-six military stations, having an aggregate mean strength of 4,395 officers and enlisted men, there were, during the four years, 1,043 cases of remittent fever with three deaths, and 4,892 cases of intermittent fever *with no deaths.*

Let us compare these figures, which represent the sickness and mortality from malarial fevers at a considerable number of widely scattered military stations, many of which are in decidedly malarious localities, with the mortality returns of New York, a closely built city situated upon a peninsula, and having but little land uncovered by buildings and pavements, with the exception of a narrow margin on the north in the direction of its growth. If malaria is as prevalent in this great city as at the military stations in the Division of the Atlantic considered together, more than one in twenty of its population should suffer from remittent fever each year, and more than one in four from intermittent fever. But the mortality from remittent fever should not exceed 2.86 per thousand cases, and from intermittent fever it should be *nil*.

According to Dr. Simon Baruch, of New York, who has recently contributed a valuable paper upon "Malaria as an Etiological Factor in New York,"[1] the deaths from malarial fevers in this city from 1876 to 1878 were as follows:

Remittent fever	1,083
Intermittent fever	984
Typho-malarial fever	709
Congestive malignant intermittent fever	79
Congestive chill	4

Dr. Baruch remarks: "This table demonstrates that the preponderance of mortality is not in cases of congestive and malignant fevers, but in the remittent and intermittent types."

If we take the ratio of mortality determined by our army statistics, the number of deaths recorded as resulting from remittent fever should represent more than 378,000 cases. But what shall we say of 984 deaths from intermittent fever in two years in a city in the latitude of New York, when not a single death occurred in 4,892 cases treated at military posts in the Division of the Atlantic? Again, if we refer to the seasonal distribution of the fatal cases in New York which are ascribed to malaria, we find that the general rule does not hold good which applies in regions recognized as intensely malarial, viz., that by far the largest number of cases occur during the warm months of the year, and that the inhabitants enjoy a comparative immunity during the winter season.

This is well shown by the following table and remarks, which we quote from the author mentioned:

Average Temperatures and Deaths from Malarial Fevers in New York City for 1877, 1878, 1879, 1880, 1881, *and* 1882.

Period.	Average Temperature.	Number of Deaths.
January to April	33.98°	586
April to July	60.06°	684
July to October	72.37°	954
October to January	46.14°	812

With an average temperature barely above the freezing point, we are expected to believe that New York furnishes 586 deaths in three years, or nearly one hundred deaths from malarial fevers in three months. This is a startling record, the comparison of which with the statistics of any other city of the temperate zone will demonstrate that a serious error is hidden within it. In Dr. Chaillé's[2] able statistical papers it is shown that the total mortality from malarial fevers in New Orleans from 1856 to 1860 was 1,315, and of this number 1,047 were reported from May to October (inclusive) and 268 from November to April (inclusive), affording evidence of the fact that even in semi-tropical New Orleans the winter mortality from malarial fevers is as one to about four of summer mortality, while in New York City the summer and winter mortality from the same diseases are nearly equal.

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[1] The Med. Rec, N. Y., November 10, 1883.

[2] N. Orl. M. & S. J., 1870, xxiii.

It would be a hopeless task to attempt to determine the true nature of the fatal forms of disease which are included in these mortality returns of the great city of New York, but it is evident that a certain proportion of the cases at least are improperly ascribed to malaria, if the term is given its restricted and generally accepted signification.

There is no reason to suppose that the physicians of New York are less expert in diagnosis than those of other sections of the country, and if, as we suppose, the *city* malaria, which kills, is different from the *country* malaria, which produces periodic fevers curable by quinine, the error in diagnosis is not confined to this city, but is wide-spread, and arises from the mistaken belief that one and the same poison gives rise to two classes of fever, which, however nearly they may resemble each other in semiology, have a different etiology.

Sydenham has said: "All diseases ought to be reduced to certain and determinate kinds, with the same exactness as we see it done by botanic writers in their treatises of plants. For there are diseases that come under the same *genus*, bear the same name and have some symptoms in common, which, notwithstanding, being of a different nature, require a different treatment." In most text-books the effort is made to reduce diseases to "certain and determinate kinds, with the same exactness as we see it done by botanic writers." But unfortunately in practice the typical cases of these several species of disease are often difficult to find, and it is the numerous atypical cases which puzzle the diagnostician. So, too, the student of natural history often finds it difficult to make the plants he finds in his travels fall into the specific niches which the systematic botanist has constructed to receive them. The truth is that all systems of classification, either of diseases or of plants, are in a certain degree arbitrary and artificial, for nature is continuous, and it is as impossible to draw a sharp dividing line between the animal and vegetable kingdoms, for example, or between the algæ and the fungi, as between daylight and darkness. We believe, nevertheless, that the poison of intermittent fever is one thing, the poison of enteric fever another, and that of yellow fever still another. But that these several disease-poisons are identical at all times and under all circumstances would be too much to assert in view of the varied effects which they produce. Indeed, we have no evidence that the various types of disease which are recognized as malarial, for example, are all due to a single poison. If we look at the matter from the point of view of the germ theory, it would rather seem as if these diseases constituted a genus, and that several allied species of micro-organisms are concerned in their etiology rather than that all are due to a single species. Or at least, if we do not recognize the value of specific distinctions among these lowly organisms, we must admit that the single species readily undergoes modifications as a result of changes in conditions relating to its environment.

It is generally assumed that the intermittent and remittent forms of malarial fever are due to the same cause, and the difference in type is supposed by some to be a difference in degree only; the remittent being a manifestation of exposure to the poison in a more intense form. This view seems to receive support from the fact that during convalescence from remittent, intermittent attacks often occur. But it must be remembered that in malarious regions similar attacks frequently occur during convalescence from other diseases as well.

Sir Joseph Fayrer, in his recent work on the "Climate and Fevers of India," says: "Remission and intermission, however, are not to be regarded as absolute indications of degree of intensity, for a remittent may be comparatively mild, while an ague may become pernicious." This author, however, regards the types of malarial fevers as "only different modes of expression of the same thing," and according to him, "such terms as jungle fever, Terai fever, Bengal fever, Deccan fever, etc., merely express local varieties with no fundamental differences, though there may be certain subordinate features which distinguish each, depending on the local climate and meteorological conditions."

Whether conditions relating to climate and local surroundings act upon the cause or upon the patient in modifying the type of malarial diseases is an unsettled question. Probably they act in both ways.

Although intermittents and remittents occur side by side in many parts of the world, the seasonal and topographical prevalence of these two forms of fever is not in all cases identical. According to Griesinger, in districts where malaria is endemic the remittent variety prevails in the humid coast regions, and ordinary remittent on higher lands. This difference is ascribed to "the varied intensity of the morbific agent." Fayrer says that the malaria of Terai or Sunderbunds causes dangerous remittent; that of the general surface of Bengal, ordinary ague or milder remittent; and asks the question: "Is that which causes jungle fever, bilious or ordinary remittent, simple ague, cachexia and neuralgia, one and the same, or is it of different kinds?"

In commenting upon this question the remark is made: "Unless it be proved that malaria is due to organisms we know nothing of its essential nature." But the final conclusion is reached that "excluding individual predisposition, we are probably justified in assuming that different degrees of intensity or concentration of the miasm produce the different effects." Morehead, in his "Researches on Disease in India," observes that "when the conditions of malaria exist in great degree, remittent fever prevails; but that when these lessen the type becomes intermittent." Dr. Chevers, in his recently published "Practical Notes on the Ordinary Diseases of India," remarks as follows:

> The questions, How far are intermittents and remittents allied in etiology? and, Is one of these types of fever convertible into the other? are, although very interesting, of no great practical importance, except to those who consider that remittent fever is either typhus, enteric, or relapsing fever. My own opinion, founded upon much observation and thought, is that they are cognate but perfectly distinct maladies, caused by different kinds, degrees, or forces of malaria, not always prevailing in the same district, and generally appearing at different seasons of the year; the intermittent being a disease of swamps and marshes, the typical remittent a malady of jungles and terais. . . . I believe, almost to certainty, that intermittents and remittents are not degrees of development of the same malady or the results of one and the same cause.[1]

The writer is glad to see this view formulated in so definite a manner by one who has had such extended opportunities for observation. The question is certainly worthy of further consideration. At the same time it must be admitted that the malarial intermittent and remittent fevers are so closely allied clinically that it is at present difficult to see how they can be divorced etiologically. We recognize, however, that "remittent fever" is a very comprehensive term, and that not all fevers which are called by this name, and in which the pyretic movement exhibits a remittent character, are truly malarial in their origin.

Where two or more endemic diseases occupy the same territory, questions

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[1] Lond. Med. Times and Gaz., February 10, 1883, p. 149.

relating to etiology and to diagnosis often become so complicated as to lead to great confusion.

This results from the frequent occurrence of atypical cases of each specific disease, and from the modifying influence of one disease-poison upon the course of an attack induced by a different one.

This general proposition is illustrated by the various opinions held by medical authors in all parts of the world, as regards the etiology of certain forms of fever which occur in those localities where typhoid and malarial fevers are both endemic, and also by similar differences of opinion as regards the etiology of yellow fever in regions where it exists as an endemic disease, which are commonly regions where the malarial poison is also evolved in abundance.

The view that endemic diseases occurring in the same area are due to a single cause, especially when the symptoms are somewhat similar, is a natural one, and is commonly accepted in advance of precise observations relating to clinical history, mode of origin, etc. But with the advancement of science differentiation occurs. Thus it is now well established that yellow fever is due to a specific poison, the production and dissemination of which is governed by different laws from those which control the evolution of malaria. But for a long time a majority of the physicians in our Southern seaport cities, where yellow fever as a result of importation was of almost annual occurrence, maintained that this disease was endemic in these cities; and not a few insisted that it was simply a severe form of malarial fever, produced by the same poison which gave rise to the intermittents and remittents, which as they pointed out often occurred in the same localities and at the same time.

Quarantine, and sanitation by excluding yellow fever from these cities, except as an occasional visitor clearly introduced by importation, has made this view untenable in the United States, but it is still held by a considerable number of physicians in the West Indies. Aiken, who wrote an account of this disease, not from personal observation, but from a study of the literature available at the time he wrote, says: "No dividing line can be drawn between the several forms of malarious fevers and malarious yellow fever." That this opinion still prevails is shown by the following quotations from more recent writers.

Staff-Surgeon Johnson, of the British army, in giving an account of an outbreak of fever at Trinidad, West Indies, in 1869, says:

> The general tendency of ague, when present, seemed to be to pass into remittent, and remittent into yellow fever. . . . To find a general title which shall stand for the variety of fever seen in this outbreak is of course impossible, but the prevailing type is not inaptly represented by the term "typhoid bilious remittent,". proposed by the Surgeon-General of the colony. Perplexed by the great and sudden prostration, which tended to hurry certain cases to a fatal termination, practitioners, despairing of a more exact designation, were content, in some instances, to return the disease as "malignant fever;" and however indefinite and unsatisfactory such a name must be admitted to be, there is still some excuse for its employment. The paroxysmal character, never very well marked, was for instance, say, altogether obscured. There might have been yellowness of the skin without black vomit, or black vomit without yellowness of the skin, and the aggregate of the symptoms did not appear, perhaps, to justify the title of yellow fever, but the disease required some name. . . . When the distinction was established between specific and malarious yellow fever, a great benefit was conferred upon practitioners in the western tropics, who were thereby relieved from many perplexities of diagnosis. . . . Few facts are better recognized among medical men in this colony than that they have frequently seen remittent fever pass into yellow fever, or what they would have called yellow fever had they not been checked by passages similar to the following: "The progress of inquiry has entirely

> disconnected true yellow fever from malaria." "The two agencies of yellow fever and paroxysmal fever are entirely distinct." . . . We have lately had under notice in this locality the following varieties of fever, partially concurrent or sequent: 1, Simple continued fever; 2, ague; 3, remittent fever; 4, malarial yellow fever; 5, specific yellow fever.

In the same report, Assistant Surgeon Jameson, of the 47th Regiment, says:

> The cases in which much albumen, hemorrhage, yellowness of the skin, or black vomit were present, were returned as yellow fever. Those cases in which even imperfect remission could be observed, and in which the symptoms of blood-poisoning were less pronounced, and the urine was free from albumen, were returned as "remittent," and those having no appreciable paroxysmal tendency, and in which the symptoms were of still less severity, as continued fever. . . . That the different forms of fever thus designated, even those returned as continued fever, had a common malarial origin, may be looked upon as certain, the tendency being for the cases described as remittent to pass into continued, those of continued into yellow fever, and the latter into ague. . . . Quinine was found to have no curative influence in the cases of malarial yellow fever in which it was tried. On the contrary, from my own observations and those of others, I should say its administration aggravated the symptoms; thus another method of distinguishing between this malady and specific yellow fever proved inefficacious.—Appendix to "English Army Medical Department Report for 1869."

The confusion into which these English army surgeons fell as regards the etiology and differential diagnosis of malarial and yellow fevers is not surprising, and is but a repetition of a mistake which has been made many times in regions where both of these diseases are endemic, or where, from frequent importation, yellow fever is looked upon as a disease of the country. At the outset of nearly every epidemic of yellow fever in our southern seaports, similar mistakes were formerly made, and this not by a few individuals but by the profession generally. In New Orleans, for example, just before the acknowledgment is generally made that yellow fever prevails, the weekly mortuary reports commonly show a great increase in the number of deaths from malarial fevers. But when it is generally admitted that the prevailing disease is yellow fever, the deaths from remittent fever, congestive fever, and pernicious fever fall off in a notable manner.

Mild epidemics of yellow fever, having a low rate of mortality, are especially liable to be pronounced malarial fever.

Bérenger-Feraud, whose scientific attainments and opportunities for the study of yellow fever, both in the French Antilles and on the coast of Africa, entitle his opinion to great weight, believes the fever known upon the islands of Gaudeloupe and Martinique as *fièvre inflammatoire*, etc., to be nothing more nor less than a mild form of yellow fever. He says:

> Certainly, for unprofessional persons, the *fièvre inflammatoire* is absolutely different from yellow fever, for the important reason, as they say, that in one recovery is the rule, almost absolute, whilst in the other, one-quarter, if not one-half of those attacked succumb. This reason may appear sufficient for those who are not familiar with the study of disease, but is it as convincing to us? No! And if we admit, for example, that there is between the two diseases a simple difference of intensity, the question of great mortality on the one hand, and extreme benignity on the other, no longer prevents the union of the two diseases in a single group.

The difficulties of diagnosis arise, not in the well-marked and fatal form of the disease, but in these milder epidemics which, when they occur among a creole population, are so easily confounded with other endemic or epidemic febrile disorders. It is doubtful whether these difficulties can be overcome, by any amount of professional acumen, upon a simple clinical inspection of the cases, and it will often be necessary to take into consideration the facts relating to the origin and progress of an epidemic in order to arrive at a just conclusion as to its etiology.

If we turn from the yellow fever zone to the East, we shall find that other forms of continued fever, which are endemic in the malarious plains of India and elsewhere, are equally the cause of confusion and of differences of opinion among physicians as regards questions of etiology and diagnosis. Thus Parkes says, in the "English Army Medical Report of 1870" (Appendix, p. 239): "At the present time in India an opinion seems to be gaining ground that the prevalent notions about malaria require to be reconsidered; that 'malaria' is much less common than is supposed; and that the mixing up of relapsing fever, typhoid fever, and perhaps other specific fevers, with malarial diseases has caused so much confusion that all old observations should be thrown aside, and the subject again investigated from our present stand-point of diagnosis of fevers."

Russell, in a paper published in the "Transactions of the Epidemiological Society" (vol. iv., p. 547), says: "The pyrexia of true non-malarious typhoid often so closely resembles that of true malarious remittent fever, that in India the diagnosis between these two diseases is frequently extremely difficult, and must be decided by other distinctions than the types of their pyrexias."

Sir Joseph Fayrer, in his Croonian lectures, says: "In typical cases of remittent the diagnosis is clear enough, but in many others it is difficult, if not impossible, for the characters of the temperature curve vary so little that it is not possible to deduce from them any certain differential points of diagnosis."

By referring to the periodical literature relating to fevers, we shall find that the same confusion exists in our own country, and that the most diverse opinions are entertained as regards the etiology of the endemic febrile disorders of a continued type. These are widely distributed, and present different aspects at different times and places. As in India, they have in some instances received local names; and, as in India, they are all ascribed by some practitioners to the one cause, malaria. This is a very simple solution of the etiological problem, but can hardly be considered satisfactory or scientific, inasmuch as we do not even know what "malaria" is. But using the word as the name of a specific agent which produces that well-defined class of paroxysmal fevers known as intermittents, we have to inquire what other morbid phenomena are produced by the same cause.

And first let us consider what tests we have for the recognition of the hypothetical agent malaria.

The most marked characteristic of the fevers recognized everywhere as malarial, is indicated by their name, intermittent. But it must be remembered that intermittence is not peculiar to malarial fevers.

Sir Charles Murchison gives the following as the principal causes of intermitting or paroxysmal pyrexia:

1. Malarious intermitting fever (true ague).
2. Certain cases of typhoid or enteric fever.
3. Certain cases of relapsing fever.
4. Pyæmia.
5. Fever from pent-up pus independent of pyæmia.
6. Fever from ulcerative carditis, with or without embolism.
7. Tubercular fever.
8. Fever from lymphadenoma.

9. Syphilitic fever.
10. Urinary intermitting fever.
11. Hepatic intermitting fever.
12. Intermitting fever from morphia.

The remark is made that in pyæmia the paroxysms, though often irregular, are at other times remarkably periodic. Ulcerative endocarditis now and then gives rise to an intermitting fever which may recur daily for weeks, or even for months. In lymphadenoma the paroxysms are usually quotidian, and may recur for weeks; in some instances they are made up of three distinct stages—of rigors, heat, and sweating. The same author says: "Even the so-called continued fevers are more or less remittent."[1]

Harley says: "One of the most general facts observed in reference to enteric fever is the frequent occurrence of intermittence in the pyrexial condition."[2] Trousseau remarks that "enteric fever may simulate, at first, intermittent fever."[3]

These authoritative statements, which might be greatly multiplied, show that an intermittent or remittent pyrexia cannot be taken by itself as evidence of malarial poisoning.

What test have we then? The present writer knows of none of universal application, unless the curative power of the cinchona alkaloids be accepted as such a test. But, while it is very generally admitted by practitioners in malarious regions in all parts of the world that these alkaloids cure malarial intermittent fevers, even of the gravest type, it is also in evidence that they do not cure other fevers ascribed to malaria. We must therefore admit that this test is not reliable, or that the fevers which do not yield to quinine have a different etiology from those which do. A third possibility worthy of consideration is, that the malarial fevers which do not yield to quinine are complicated by organic lesions, the result of the action of the malarial poison, which require time for their restoration. Of course, any complication resulting from the action of a different specific disease-poison, removes the case at once from the category of strictly malarial fevers.

It is evident that the quinine test, which without doubt is of great value even if we cannot accept it as a universal touchstone for the differential diagnosis of malarial fevers, must be applied with great caution. For this remedy is of decided benefit in the various forms of septic poisoning, which, as pointed out by Murchison, often exhibit an intermittent pyrexia. And also in certain ephemeral fevers evidently not due to malaria, *e.g.*, thermic fever. Moreover, there is always liability to error in ascribing to the remedy a recovery which may have taken place quite independently of it. Thus in mild cases of a specific continued fever of brief duration, such as yellow fever, recovery occurs promptly, without special medication. But very many practitioners, when this disease prevails, adapt the routine practice of giving quinine in every case of fever which falls into their hands, and these gentlemen often take great credit to themselves for having promptly cured their patients, when one familiar with the natural history of the disease would say rather that the patient had recovered in spite of the remedy.

If we have no test which enables us to decide definitely, under all circumstances, whether a fever is or is not of malarial origin, there is at least no difficulty in diagnosing the typical intermittent fevers, in which a well-marked paroxysm occurs daily or every second day; and we must insist that the prevalence of this form of fever, at least during certain seasons of the year, be taken as a test of the presence of the kind of malaria at present under consideration, in any particular region. That other kinds of malaria may produce other forms of fever is beyond question. Thus we have a malaria of yellow fever, and of influenza, and of cholera, etc. But the question is, whether this kind of malaria produces other forms of fever, and especially whether continued fevers not curable by quinine are caused by this same malaria.

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[1] Lancet, Lond., May 3, 1879.
[2] Reynolds' System of Medicine, vol. i., p. 389.
[3] Clinique Medical, 2d ed , p. 247.

It is evident that a systematic account of malarial diseases cannot be undertaken without a preliminary consideration of this question. The author, therefore, proposes to pass in review, in as brief a manner as is consistent with his purpose, the various diseases which have been ascribed to malaria.

Ephemeral Fevers or Febricula.

Ordinary intermittent, unless arrested by treatment, usually consists of a series of paroxysms, and when arrested there is a tendency to recurrence at certain stated intervals. Whether an ephemeral fever of a single paroxysm is a common result of the action of the same cause is open to question. We have ample evidence that ephemeral fevers may occur in non-malarial localities from a variety of causes. In malarious regions, however, it is quite the fashion to attribute every case of ephemeral fever to malaria.

Fayrer says: "A mild form of simple fever is of frequent occurrence in India, which is due to ordinary causes, such as changes of temperature, excesses in eating or drinking, fatigue, excitement, disordered secretion, or functional derangement of the abdominal viscera. It is most frequent in the hot seasons, but may occur at any time. When it happens in persons newly arrived in the country, it is probably free from any malarial taint, though the onset may resemble ordinary ague."[1] Most people soon after arrival in India are said to suffer from fever of this character, and as a general rule recovery occurs within a few days as a result of simple treatment, consisting in the administration of an efficient purgative, diaphoretic medicine, tepid sponging, a restricted diet and rest. Similar attacks are quite common in the West Indies and in tropical and semi-tropical countries generally. That they are not due to malaria is proved by the fact that they occur in localities where true malarial fevers are unknown, at Bermuda for example; that persons on shipboard, removed from any malarious influence, may be attacked; and, in general, that they may commonly be traced to the causes mentioned by Fayrer, and occur quite as commonly among the denizens of cities where intermittent fevers of local origin are rare, as among those residing in the country.

In addition to the causes above mentioned it is probable that ephemeral fevers may result from the ingestion of septic material, not having specific characters, either in food or drink; and perhaps from putrefactive decomposition in the alimentary canal, resulting from the action of septic organisms upon food taken in excess of the requirements of the system and of the digestive capacity.

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[1] Sir Joseph Fayrer, M.D., F.R.S., etc.: On the Climate and Fevers of India; being the Croonian Lectures delivered at the Royal College of Physicians in March, 1882, p. 155. London: J. & A. Churchill. 1882.

Again, there is reason for believing that ephemeral fevers may result from the action of specific disease-poisons, such as that of yellow fever or of dengue, when individuals who have but slight susceptibility to these diseases come within the range of their epidemic prevalence ; or where the exposure has been slight.

Continued Fevers Ascribed to Malaria.

The nomenclature of diseases recommended by a joint committee appointed by the Royal College of Physicians of London (published in 1869) includes Simple Continued Fever, with the definition, "continued fever having no specific character."

The same heading was included in the nomenclature employed in the Quarterly Returns of Sick and Wounded used in the United States Army, prior to June 30, 1862. Subsequently to this date a new nomenclature was employed, in which this heading no longer appeared, and in place of it was Dr. Woodward's newly coined term "Typho-malarial fever." As a result of this change the cases which had previously been diagnosed as common continued fever, necessarily found a place under the headings "typhoid fever," "typho-malarial fever," and "remittent fever."

Woodward says, in his "Camp Diseases," published in 1863 : "Typho-malarial fever is the characteristic camp fever of the army at the present time, and has been so since the commencement of the war. Cases of ordinary typhoid, unattended with malarial phenomena, undoubtedly do occur. *Much more frequent are malarial fevers which in their course assume a continued form without presenting the abdominal symptoms of true typhoid disease and without exhibiting in fatal cases the characteristic intestinal lesion.*"

We shall have occasion to speak of typho-malarial fever later. The questions we wish to consider at present are : Whether there is a common continued fever not malarial or typhoid ; whether the cases of remittent fever which assume a continued form are properly ascribed to "malaria" in the first instance ; and if so, whether this is the only factor concerned in their etiology.

According to Morehead "the common continued fever which occurs in many parts of India in the hot, dry months of the year, chiefly in April and May, in its most aggravated form in recently arrived robust Europeans, often favored by intemperance and fatigue, also requires to be distinguished from remittent fever. . . . If the attack be in a hot and non-malarious season, in a recently arrived European, and the febrile excitement be high and continued, there need be no hesitation in considering the disease to be continued fever, not malarious remittent."[1] Turning to another page in the same volume, we find that the common continued fever to which Morehead alludes is a fever of brief duration and that it really corresponds with the ephemeral fevers or febricula of other authors. He says : "The mildest variety—ephemeral—may proceed from any of the ordinary exciting causes which have been mentioned, and though most common in unseasoned Europeans, may occur in natives as well as in Europeans who have been some time resident in India. It consists of febrile symptoms without local complication, commencing with chills, followed by reaction, and this by perspiration, and thus is removed in from twenty-four to thirty-six hours. But the febrile reaction may continue for four or five days, and then the term *common continued fever* is more correctly applied" (p. 163).

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[1] Clinical Researches on Disease in India, p. 57. 1860.

That the form of common continued fever here referred to is not due to malaria, seems to be proved by the fact that it occurs where malarial fevers are unknown. Thus, several writers agree that malarial remittents and intermittents are never met with as indigenous products of the Bermudas. But we learn from a report of Assistant-Surgeon Don, of the English Army, that continued fevers of brief duration are common. He says:

> As in the tropics and sub-tropics all the world over various forms of continued fever are met with at certain seasons of the year, so in Bermuda. During the hot season occur many cases of febricula and simple continued fever, which vary very much both in intensity, and duration of symptoms. . . . The "continued" forms of fever in Bermuda may appear as merely exaggerated and lengthened febricular attacks, or in some cases be prolonged for ten or fifteen days, and in a few may be still further prolonged and associated with low, typhus-like conditions of the vital and intellectual functions. . . . I mention these forms of fever in order that the enteric continued type may appear in due relation to them, and also to show that it is indeed a matter of no small difficulty to draw a sharp scientific line, either in practice or theory, between the different forms of continued febrile disease as seen in such a climate as that of Bermuda. Moreover, the various forms of continued fever are there seen occurring side by side, and apparently originating under precisely similar circumstances. . . . I am recording the experience of all when I state that on a case presenting itself, it is often exceedingly difficult to pronounce with any degree of certainty on the exact type, whether in fact it may prove a simple continued case, or one which ultimately may be complicated with bowel lesion.[1]

As already stated, the fact that malarial remittents and intermittents do not occur in Bermuda has been recorded by several writers. This evidence, therefore, relating to the prevalence of continued fevers of brief duration side by side with an endemic enteric fever, is of very great value as showing that these fevers are not malarial in their origin. In malarious regions, however, these continued fevers are very commonly ascribed to the action of malaria. Thus Fayrer says:

> Writers on Indian and tropical disease have described a form of continued fever liable, like remittent, to be modified by visceral complications, and to have a fatal termination, post-mortem examination revealing pathological changes of various degrees of importance. It is attributed to climatic causes, and the circumstances attending life in tropical and subtropical regions, such as heat, atmospheric vicissitudes, *terrestrial emanations*, personal habits; and no very distinct characters differentiate it from remittent when it has assumed a continued form. Twining, Annesley, Martin, and others refer to such a fever, and generally, I think, they regarded it as a variety of malarial fever, in which, perhaps, there is little difference of opinion. But it is necessary to distinguish it from specific continued fevers, with which it may be confounded. In typical cases of remittent, the diagnosis is clear enough; but in many others it is difficult, if not impossible, for the characters of the temperature curve vary so little that it is not possible to deduce from them any certain differential points of diagnosis.[2]

That these continued fevers are due to "terrestrial emanations," and therefore constitute "a variety of malarial fever" in the sense in which Twining, Annesley, and Martin would have used the word malarial, is quite probable; but that they are due to the same malaria as that which produces paludal intermittents and remittents is open to serious question.

In the first place, we would call attention to the fact that malarial fevers, properly so called, have a tendency to recur, whereas these continued fevers of warm latitudes are generally known as acclimating fevers—

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[1] English Army Medical Department Report, 1869, Appendix, p. 380.

[2] Op. cit., p. 163.

that is to say, a stranger is likely to suffer an attack soon after his arrival in the regions where they prevail; but having suffered an attack he is acclimated, and, to a certain extent, protected from subsequent attacks. This protection, as a result of a single attack, is the rule in the case of the specific continued fevers, whereas an attack of malarial fever predisposes to a second attack. This circumstance, and the fact that these fevers are not cured by quinine, considered in connection with the evidence relating to their prevalence in Bermuda, where true malarial fevers are unknown, seems to demonstrate conclusively that these fevers should be excluded from the category of malarial diseases. The question whether they are due to the action of the specific poison of typhoid we cannot stop to discuss; but we venture the opinion that a certain proportion of these cases at least are abortive cases of typhoid. Others we believe to be due to poisoning by septic material of non-specific character. Others, still, are due solely to the combined influence of heat, imprudence in diet, the use of spirituous liquors, excessive fatigue, etc.

Continued Remittent Fevers.

When a remittent fever is complicated by serious visceral derangements, functional or inflammatory, it may continue, in spite of the administration of quinine, until these are relieved. The complication may consist in a certain degree of gastritis, or gastro-enteritis, the coexistence of dysentery, or, more commonly, in serious derangement of the hepatic function. But when a remittent fever, not complicated in this way, resists the curative action of quinine and assumes a continued form, the probability is that it was not a truly malarial remittent in the first instance, or that there is a second etiological factor to which the continued form is due.

Probably one of the most common mistakes in diagnosis, made in all parts of the world where malarial and enteric fevers are endemic, is that of calling an attack of fever, belonging to the last-mentioned category, remittent. This arises from the difficulties attending a differential diagnosis at the outset, and from the fact that having once made a diagnosis of remittent, the physician, even if convinced later that a mistake has been made, does not always feel willing to confess it. The case therefore appears in the mortality returns if it prove fatal, or in the statistical reports of disease, if made by an army or navy surgeon, as at first diagnosed. Quite as frequently, perhaps, the physician remains convinced that his first diagnosis was correct, inasmuch as the fever was decidedly remittent in type during the first week, and is puzzled to know why he did not succeed in arresting the progress of the disease by the free administration of quinine. By referring to the literature of the subject he will find ample support for the view that remittent fevers are likely to assume a continued form, and that patients suffering from malarial fevers of a remittent or continued type frequently fall into a typhoid condition. It is therefore not surprising that mistakes are frequently made, especially when we remember that during the first week typhoid fever has a decidedly remittent character, quite independently of any malarial complication,[1] and that the periodic fluctuations of the pyretic movement are still more pronounced when it occurs in a malarial subject, *i.e.*, one who has suffered frequent attacks of periodic fever. Moreover, there are undoubtedly cases of enteric fever of so mild a form that all of the characters commonly relied upon for making a diagnosis are wanting, and these cases of typhoid poisoning may be complicated by the most decided evidences of malarial poisoning when the case occurs in a malarious region, or in an individual who has been recently exposed in such a region.

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[1] See Wilson: The Continued Fevers, p. 148, Wood's Library, 1881.

It is also pretty well established that a non-specific continued fever may result from exposure, in overcrowded and illy ventilated apartments, to the noxious emanations given off from healthy human bodies—crowd poison—and from decomposing animal matters in cesspools, sewers, etc., the idio-malaria of Dr. Edward Miller. This kind of malaria has been denominated *civic* malaria, and there is no objection to this term, if we are at the same time permitted to qualify our *malaria* by the adjective paludal. But the objection is raised that this implies that it originates *only* in swamps, which is not true. If, therefore, we admit the force of this objection we are reduced to the necessity of using the word malaria by itself to indicate the toxic agent which produces the periodic fevers, and as this use of the term has the precedence, and is generally adopted by medical authors, we must object to the indiscriminate use of the term which is now so largely made, especially in those portions of the United States where malarial diseases, properly so called, are comparatively rare.

Evidently the term "civic malaria" is open to the same objection as has been raised against "paludal malaria." This kind of bad air is not alone generated in crowded cities; it may also be encountered in its most atrocious and concentrated form in country villages, and even in the hut of the agricultural laborer and in the dug-out of the mountaineer or miner.

We shall now proceed to consider the facts relating to certain forms of continued fever commonly ascribed to the influence of malaria, and which are known by local names in various parts of the world.

Naples Fever.

Dr. Borelli,[1] Professor of Medicine in the University of Naples, has given a very interesting account of this fever, which by many is ascribed to malaria. According to this author cases of true malarial infection, of well-pronounced type, are rare in the interior of Naples, whereas the so-called "Naples fever" prevails most extensively in the central portion of the city. The opinion is expressed that typhoid infection is at the root of this form of infection, which exhibits every grade of violence from the mild and abbreviated forms, to which the name febricula is given, to complete and relatively severe typhoid. In all of the varieties *intermittence* is a symptom repeatedly observed. Dr. Borelli says that if the febrile intermittence depended upon a malarious element, the salts of quinine ought to cure it rapidly, yet they invariably fail, and remarks further that:

"In paludal infection, when the fever assumes a quotidian type, each fresh access almost invariably begins during the forenoon; whereas in intermittent typhoid, the type, although quotidian, has an evening rhythm—that is to say, the exacerbation occurs in the afternoon or evening, so that in that respect it resembles all those spurious intermittent fevers which accompany the other diseases that I have mentioned"—tuberculosis, caseous inflammation of the lungs, chronic inflammations of serous membranes, pyæmia, etc. We may remark that, in general, all forms of septic poisoning give rise to fevers having an intermittent or remittent type.

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[1] Med. Times & Gaz., Lond., July 8, 1876.

Roman Fever.

If the "Naples fever" is essentially typhoid, we are assured by two very competent authorities, Sullivan and Colin, that "Roman fever" is a strictly malarial fever. According to Sullivan, typhoid fever is endemic at Naples, and eighty-five per cent. of the cases which occur in Rome are imported from that city, or from other Italian cities.[1]

M. Colin, physician in chief of the French army, observed these fevers during the French occupation of Rome. In his treatise ("Des Fièvres Intermittentes"), published in Paris in 1870, he says: "During the time of our occupation of Rome, the summer remittent fevers constituted the first phase of the annual endemo-epidemic. During sixteen years we were able to verify the remarkable regularity of the recurrence of the date of their explosion; the first cases appeared, almost at a fixed day, toward July 5th or 6th; then the number of those admitted to hospital attained its maximum toward July 20th; it maintained itself at this level until about August 20th, when a movement of decline occurred so rapid that at the end of this month the remittent fevers became relatively rare; and during the month of September they were usually represented by a few cases only, which were lost, so to speak, in the immense number of cases of intermittent fever." Colin remarks that these fevers are not so common in the central part of the city as in the suburbs, and that soldiers residing in Rome were more subject to attack during the second or third year of their stay than during the first. The types described are designated "gastric," "bilious," and "pernicious." The varieties of pernicious fever are included under eight heads, viz.: "Comatose, deliriant, convulsive, algid, choleraic, icteric (hemorrhagic), diaphoretic, cardialgic, and syncopal." These names all indicate that the pernicious character depends upon an intense degree of poisoning, by which the central, or the ganglionic nervous system is, as it were, overwhelmed. But our author adds to this list two other forms of pernicious fever which he denominates solitary, meaning, I suppose, that the cases do not occur in groups. These are called "summer and autumnal sub-continued fevers." In relation to these he remarks: "From the preceding facts we are forced to the following conclusions: Between the summer and autumnal sub-continued pernicious fever and typhoid fever there is a symptomatic connection, such that it often defies all attempts at differential diagnosis; often, even, there is no occasion for a differential diagnosis, the pernicious remittent being identical, anatomically, with typhoid fever in a great number of cases."

Sullivan, also, refers to a sub-continued fever as occurring in Rome, and is at considerable pains to establish a differential diagnosis between this form of fever and typhoid. He designates it "pernicious pseudo-typhoid" and speaks of it as the so-called "Roman fever." We conclude, then, that this is the "Roman fever" which travellers so much dread, and we take the liberty of doubting whether it is properly classed with strictly malarial fevers, as Sullivan contends. We are rather inclined to the view taken by the learned Professor Bacelli, of Rome, who holds that "this fever may be a combination of two elements, giving rise to a two-fold morbid process, to lesions of a two-fold nature, coexisting in the same organism, one occasionally getting the better of the other. Although from the mode of invasion of the fever we might be inclined to suspect its double origin, we should soon detect on careful examination, that one poison is more potent than the other, and that is always the typhoid, but not to such an extent as not to allow the malarial element to peep through, especially at the beginning and decline of the fever." In other words this would appear to be a fever identical with that which Woodward has designated typho-malarial.

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[1] Med. Times & Gaz., Lond., January 12, 1878.

Malta Fever.

The medical officers of the English army stationed at Malta have described a peculiar form of fever, which by some is attributed to malaria. A similar fever prevails at Gibraltar. According to Professor McLean, this is a typho-malarial fever, but other observers fail to find any evidence that it is due to the same poison which produces specific enteric fever. Thus Professor Veale[1] says: "That it is not our enteric fever appears certain, from the fact that it has neither its clinical form, nor its mortality, nor its specific anatomical lesion; that it is not malarial fever seems proved by its absolute resistance to quinine, by its protracted duration after removal of the sufferers from a malarial locality, as well as by its different aspect and progress throughout." The following account of the disease is given by Veale:

> Its commencement may occasionally have some resemblance to mild quotidian ague, but more frequently the invasion is so insidious that the patient is unable to mention the day on which his illness began. He usually first complains of a feeling of lassitude and drowsiness, with slight headache and loss of appetite. After a few days he perhaps thinks he is bilious; he has nausea, sometimes even vomiting, and his bowels are either costive or too loose. He seldom has rigors at this stage, but he is chilly and feverish and he feels that his illness is increasing day by day. His headache grows worse and affects his forehead especially; his lassitude and debility become so great that he ceases to take interest in anything; he loses his appetite altogether; and throughout the whole day and night he remains hot, thirsty, ill, and desponding. If the case is a mild one these symptoms decline after a variable period, rarely less than a week, more frequently extending to two or three, and the patient fancies himself convalescent. Sometimes he leaves the hospital and goes to duty, but after a day or two he finds his old symptoms coming on again, his nausea or vomiting returns, with loss of appetite and irregularity in the action of the bowels. Very frequently he now suffers from one or two attacks of diarrhœa, and occasionally this assumes a dysenteric character, being attended with much tenesmus and the passage of mucus more or less tinged with blood. Sometimes he thinks he catches cold, for he begins to cough and has flying pains about the chest; and after a time it may be observed that his sputum is tinged with blood, or he may be seized, sometimes very suddenly, with a pain in his back or in one of his limbs, and this pain holds him as if in a vise, it is so severe. During all this time he has been losing flesh steadily; he has now become very anæmic; his hair falls out; his spleen, and sometimes his liver also, become enlarged and painful; and it is usually at this stage that, if a soldier, he is invalided and sent to England.
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> If the case is a severe one, many or all of the preceding symptoms are aggravated. The headache becomes so intense as to be scarcely endurable; the drowsiness merges into stupor and low muttering delirium; the prostration is extreme; the lungs become greatly congested, and easily take on a low form of inflammation; there may be epistaxis, or hemoptysis, sometimes very severe; or there may be exhausting diarrhœa with occasional discharges of blood, either black or bright red; the pain in the limbs may develop into very decided rheumatism, with effusion into the joints, endocarditis, or other complications, and death may ensue at almost any period.
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> When such patients reach Netley they present a very variable appearance. . . . Nearly always there is an increase in the size of the spleen. . . . He may have dyspepsia, palpitation, pleurisy, epididymitis, or orchitis, together or in succession.

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[1] Surgeon-Major H. Veale: English Army Medical Department Report, 1879, Appendix, p. 270.

He nearly always has fever, with evening exacerbations and morning remissions, and during the night and toward morning he perspires most profusely. Such perspirations, however, bring no relief to his sufferings.

Professor Veale refers to the fact that a considerable proportion of these invalids who come to Netley from Malta and Gibraltar suffer from rheumatic affections; but remarks, "these are not cases of ordinary rheumatism."[1]

It is evident that this "Malta fever" is not a malarial fever, and this extended account of it may seem out of place in the present volume. But the writer desires, before attempting to give a systematic account of malarial diseases, properly so-called, to call attention to the various forms of pseudo-malarial fever which are most frequently ascribed to the action of the malarial poison. As regards the etiology of this "Malta fever," it would be presumptuous for the writer to attempt to solve the question when competent observers on the spot, and the medical officers of the English army at Netley, where many of the cases are sent for treatment, have failed to agree, or to arrive at any definite conclusion. The remark may be permitted, however, that these cases in their clinical history and in the nature of the complications which occur—rheumatic affections, pleurisy, endocarditis, etc.—bear a striking resemblance to certain forms of septicæmia which result from the absorption of septic products from concealed sinuses, etc., after surgical injuries. The question presents itself whether septic organisms located in the alimentary canal, or possibly in the spleen or elsewhere, may not evolve poisonous products which are the immediate cause of the various morbid phenomena observed in these cases.

Surgeon-Major Donaldson, of the English army, calls this Malta fever "fæco-malarial fever," and concludes an instructive paper in which topographical details are given, as follows: "On the whole, then, fæco-malarial fever may be supposed to be due to the constant inhalation of emanations from decomposing sewage, and to be complicated, in the majority of cases, with the poison of marsh malaria."[2]

MAURITIUS FEVER.

We read in the appendix to the "English Army Medical Report for 1871," p. 178, that "fever of a *severe and unusual type suddenly appeared* along the coast northward of the Unguini River, and as *a vessel had recently put into D'Urban from Port Louis, disabled with Mauritius fever,* the sick crew being landed at the Civil Hospital, a panic induced the Government to send down a Commission of Inquiry."

The report of this Commission, as recorded by Parkes, in the words of Dr. Cattell of the Tenth Hussars, is quite brief, and few details are given as to the character of the fever. The remark is made, however, that "the symptoms were those of bilious remittent fever in the severe, ordinary remittent in the less severe cases. In the former, especially in persons depressed by anxiety, or by alcoholism, the patient *became lemon-colored and died within six days.* In adjoining beds were the Port Louis sailors, *who exhibited exactly the same symptoms as these severe cases from Unguini.*"

The idea of importation is set aside, notwithstanding the significant facts to which we call attention by the use of italics in the above quotations, and local causes are mentioned which are believed to be sufficient to account for the outbreak. As the Port Louis sailors were sick when landed, it is evident that their sickness cannot be ascribed to local causes, yet we read that their symptoms were exactly the same as those of the severe cases from Unguini.

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[1] Op. cit., p. 265.

[2] English Army Medical Department Report, 1876, Appendix, p. 242.

In the above-mentioned report the "Mauritius fever" is only referred to by Dr. Cattell for the purpose of rejecting the theory, which had evidently been advanced by some one, that the unusual outbreak which suddenly appeared in the province of Natal, which is situated upon the east coast of Africa, could be ascribed to importation from Mauritius, an island in the Indian Ocean, about eighteen hundred miles distant. If now we seek more definite information in regard to this Mauritius fever we shall find that the importation hypothesis is not, after all, an improbable one.

We find a very satisfactory account of this fever in the "Archives de médecine navale," tome 36, 1881, written by Dr. Pellerean. In this account we are informed that the opinion was generally entertained, prior to the year 1867, that malaria did not exist at Mauritius (ancient Ile de France), but that during this year it broke out as a violent epidemic. The author's researches, however, show that malarial fevers had prevailed for many years previously, but that they were of a remarkably benign character. Looking over the records from 1820 to 1858, Dr. Pellerean ascertained that cases had continually occurred of continued or remittent type, the duration of which was from three to nine days. There was at the outset a chill—often wanting. The pulse was full and bounding, sometimes soft and compressible. There was epigastric tenderness, cephalalgia and pain in the limbs. A common character was a sub-icteric color of the skin. Excessively benign in its symptoms, this fever yielded ordinarily to an emeto-cathartic followed by 0.05 to 0.1 gram. of sulphate of quinine repeated two or three times in twenty-four hours. In a great number of cases when quinine was not administered the fever continued for some days, until the physician concluded to administer it. It occurred among all classes of the population.

There is very little difficulty in recognizing this fever as the widely known "bilious remittent fever" of southern latitudes, although no history of remissions is given. But, according to our author, the fever was not always benign. Sometimes it resisted quinine and its duration was three, four, five, or even six weeks. Hemorrhages, though not frequent, were encountered from time to time. This is a very meagre account upon which to establish a diagnosis of typhoid. But we are not prepared to assent to the supposition, which our author seems to have accepted without question, that these cases having a duration of several weeks and which resisted quinine were the same in their etiology as the "benign" cases which were promptly cured by quinine.

The violent and fatal epidemic of 1867, also, is supposed by our author to be due to the same causes which had produced the fevers prevailing prior to that date. But the remark is made: "The effects in 1867 were terrible, *and so unusual that the epidemic was ascribed to importation.*"

After the epidemic an inquiry was made which led to two official reports. One sustained the view that the epidemic was one of "malarial fever." The other ascribed it to "an incomprehensible mixture of malarial fevers and the fever of Bombay." According to one of the reporters, quoted by Pellerean, the fever manifested itself as follows:

"Suddenness of attack; the patient fell suddenly ill when in perfect health, often after a full meal. The skin became hot, *the face red, the eyes* *injected*, the pulse mounted to 90 or 100, *the skin became yellow*, the tongue dry and glassy; perspiration abundant, accompanied by a cold breath and exceedingly feeble pulse. Afterward followed intense prostration, with intolerable pain in the back, loins, and region of the liver. The poor patient, after twenty or thirty hours, died in a state of collapse similar to that of cholera. *Another character of this fever was its tendency to relapse*, to occur at all seasons of the year, in dry, elevated localities, as well as in those which were low and damp, and *to be accompanied by hemorrhages of all sorts.*"

We have additional evidence that this "malarial" fever of Mauritius was not identical with the endemic malarial fevers of the region where it prevailed as an epidemic, in the account of Barat, who states that an epidemic arose in 1869 on the Island of Réunion, which was supposed to have been "borne over by the wind from Mauritius. From April 7th to July 23d, 4,118 people, out of a population of 23,000, were attacked with the disease, and no other cause could be found for it, seeing that the state of the soil, and all other conditions that could exert any influence in its production, had remained unchanged."[1]

Who can doubt that this epidemic of 1867 was due to a new etiological element which had been introduced into this previously healthy island in the Indian Ocean? and who can help suspecting that the "unusual outbreak" at Natal, which occurred the following year, was due to the same cause; that the arrival of a ship from Port Louis, "disabled with Mauritius fever," bore a very essential relation to this outbreak? Or, who that is familiar with the clinical characters and mode of dissemination of yellow fever would hesitate to name this disease if the epidemic recorded had occurred in the West Indies instead of in the Indian Ocean?

Endemic Continued Fevers in the United States which have been Attributed to Malaria.

As in other parts of the world, so in the United States much confusion exists as to the etiology of endemic continued fevers not presenting the characteristic features of well-defined enteric fever. This difference of opinion is manifested, however, among those who contribute to our periodical literature, rather than in the writings of our standard medical authors. Thus Dr. George B. Wood, in his "Practice of Medicine" (ninth edition), commences his article on enteric fever as follows: "This is a common febrile affection, presenting a considerable diversity of symptoms, yet having, in general, a certain recognizable character, and probably constituting, in all its forms, one and the same disease. It is the ordinary endemic fever of continental Europe, and of those portions of the United States where miasmatic or bilious fevers do not prevail, and is more or less mingled with the latter within their own special limits." On another page Dr. Wood says: "In some instances, the disease presents no other symptoms than those of a moderate fever, with the characteristic phenomena of a slight diarrhœa or tendency toward it, some meteorism of the abdomen, and perhaps a few rose-colored spots. The tongue remains soft, moist, and whitish throughout; there is no vomiting, no considerable nervous disorder, no great prostration; in fine, none of those peculiar symptoms usually denominated typhous. The disease runs its course in two or three weeks, sometimes even in less time, and then subsides spontaneously, leaving no unpleasant effects. *Such cases are often mistaken for miasmatic remittent*, especially as they not unfrequently have a daily remission and exacerbation of the febrile symptoms."

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[1] Hertz, in Ziemssen's Cyclopædia, vol. ii., p. 572.

There can be no doubt that this mistake in diagnosis, which, according to Dr. Wood, was often made at the time he wrote—more than twenty-five years ago—is a very common one at the present day, notwithstanding the very definite statement of our highest medical authority, that a fever presenting the characters above given is enteric, and not malarial. Within the scope of the writer's personal observation, cases corresponding exactly with the description above given by Dr. Wood have been pronounced malarial by well-informed physicians, in and out of the army, in various parts of the country.

It is true that the diagnosis is commonly made, not from a complete clinical history of a case, but during the first week of its progress, when an exact diagnosis is, no doubt, in many instances impossible.

We find a very good account of the way in which this error in diagnosis commonly occurs in a paper on "Continued Fever in Southern Virginia," contributed to the *Virginia Medical Journal*, by Dr. Gholson, of Greenville, Va., in 1857.

> In taking a retrospect of the medical history of this region of Virginia for the last quarter of a century, the great, prominent, salient fact which arrests our attention is the change which has taken place in the profession in reference to the nature, pathology, and treatment of our indigenous fevers.
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> If it were said that at the commencement of this period there existed in the minds of the great mass of our physicians but one fever in Lower Virginia, and that bilious fever, affecting but one organ in the body, and that the liver, and requiring but one remedy, and that mercury, I fear that such a representation must be regarded more in the light of a true picture than an amusing caricature. Not only every form and variety of our ordinary periodic fever, but almost every form and variety of continued fever was too often indiscriminately regarded and treated as bilious fever. . . . Here, in Lower Virginia, the fever is of a lower grade, and frequently modified and masked by a feature of periodicity which is well calculated to mislead and suggest erroneous and frequently fatal views of its character and treatment. Sulphate of quinia in this fever has no curative power, and should never be administered except in cases clearly complicated with periodic fever; and this is no easy matter to determine in the *early period of the disease*. It is this fact which frequently makes this fever with us more fatal than it would otherwise be. A physician is called to see a fever patient in this region, suffering from fever, headache, pain in the back, etc., preceded by a chill; a slight remission or another chill is observed in a day or so, followed again by more marked cerebro-spinal symptoms. Satisfied now that this is either a case of periodic fever alone, or existing as a complication, he administers efficient doses of the quinine, feeling confident that the cerebral and nervous symptoms will rather be relieved than aggravated by the remedy. To his surprise, however, he finds he is mistaken. The cerebral disturbance grows worse, while the fever continues. With the hope of unmasking the fever and bringing out its intermittent or remittent feature, he now draws blood, and immediately administers a controlling dose of quinine and opium. Yet the fever *persists*, while the head is hot, and the mind stupid or delirious. The patient is much worse, and he now begins to suspect, when too late, that it may be a case of *continued* instead of *periodic* fever.

If now we turn to more recent authorities, we find that Wilson, in his admirable "Treatise on the Continued Fevers,"[1] says in his article upon "Enteric or Typhoid Fevers:"

> The atypical or imperfect forms constitute in most epidemics a large proportion of the cases, and when the attention of physicians is more closely turned to the study

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[1] James C. Wilson: A Treatise on the Continued Fevers. New York, 1881.

> of enteric fever from an etiological as well as from a clinical standpoint, they will be found, I believe, to be much more common where the disease is endemic than has usually been thought. The cases are partly due to mild infection, or, to use an expression already employed in this work, in speaking of other fevers, the smallness of the dose of the fever-producing principle; partly to an imperfect susceptibility on the part of the patient.

In a recent paper, "On the Mild Forms of Continued Fever which Prevail in Washington,"[1] Dr. W. W. Johnston says:

> The facts properly classified and studied in their mutual relations lead inevitably to the conclusion that there is no justice, but *positive error in affixing the term "malarial" to all negative and doubtful cases of continued fever*, as is the habit in diagnosis whenever the malarial and typhoid disease appear side by side.

TYPHO-MALARIAL FEVER.

This term, coined by Dr. Woodward in 1862, served a good purpose during our civil war, as under this heading a large number of cases of typhoid fever were included, which, in its absence from our nosological tables, would inevitably have fallen under the denomination "remittent fever." The term cannot, however, be sustained upon scientific grounds, for typho-malarial fever is confessedly typhoid fever. Woodward himself concedes that it does not designate a specific and distinct type of disease, but is simply a term which is conveniently applied to the compound forms of fever which result from the combined influence of the causes of malarious fevers and of typhoid fever.[2]

The statement that typho-malarial fever is typhoid fever—the malarial complication is admitted—is supported by a consideration of the statistics relating to the diseases of our armies in the field, in garrison, and in hospital during the late war. The statistical data upon which the following general summary is based will be found in the first medical volume of "The Medical and Surgical History of the War of the Rebellion."

White Troops in Fie!d, Garrison, and Hospital—General Summary.

	1862.		1863.		1864.		1865.	
	Number of cases.	Ratio, per cent. of cases to mean strength.	Number of cases.	Ratio, per cent. of cases to mean strength.	Number of cases.	Ratio, per cent. of cases to mean strength.	Number of cases.	Ratio, per cent. of cases to mean strength.
Typhoid fever...	21,965	7.6	32,166	4.87	10,116	1.49	9,739	1.50
Common continued fever......	11,769	4.06	....	....	....	....	....	.....
Typho-malarial fever.........	....	....	23,346	3.53	11,729	1.73	13,149	2.03
Malarial fevers (including intermittent and remittent)....	112,876	39.07	282,675	42.83	361,968	53.58	320,559	49.64
Mean strength..	288,919		659,955		675,413		645,506	

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[1] Am. J. M. Sc., Phila., Oct., 1882.

[2] Transactions of the International Medical Congress held in Philadelphia in 1876: Article, Typho-Malarial Fever.

The figures in the tables from which our general summary has been made relate to the fiscal year, which includes the period from June 30th of one year to July 1st of the following year; the data, therefore, under the heading 1862, for example, relate to the last six months in 1861 and the first six months in 1862. The change in nomenclature, made in accordance with the recommendation of a board of medical officers, of which Dr. Woodward was a member, took effect soon after the commencement of the fiscal year 1863, and it is quite apparent, from an inspection of the table, that the class of fevers previously known as "common continued fevers," subsequently fell into the group denominated typho-malarial.

The broad fact which our table shows, is that the relative proportion of cases of typhoid fever diminished and the relative number of cases of malarial fever increased as the war progressed. Thus, upon comparing the first two years with the last two years we find that the sum of the annual ratios is as follows:

	First two years.	Last two years.
Typhoid fever	12.47	2.99
Malarial fevers	81.90	103.22

This affords us a criterion for determining whether the group of fevers called, prior to 1863 "common continued fever," and subsequently "typho-malarial fever" are more nearly allied with true typhoid, or with the malarial fevers. Taking, as above, the sum of the ratios for the first and last two years of the war we obtain the following:

	First two years.	Last two years.
Typho-malarial fever	7.59	3.76

Evidently the causes which produced this group of fevers diminished as the war progressed, as did those which produced the fevers recognized as typhoid, while the relative proportion of cases of malarial fevers increased.

The etiological deduction is apparent, and the reasons for this increase of one class of fevers and decrease of another, are not difficult of comprehension. In the first place our armies moved southward as the war progressed, and came more within the influence of the malarial poison. And perhaps this general movement southward, in which, however, the Army of the Potomac did not to any considerable extent participate, carried our troops, to some extent, outside of the endemic prevalence of enteric fevers. This, however, is open to question. In the second place, it is a generally recognized fact that exposure to malaria, and attacks of malarial fevers, not only do not confer immunity but predispose to further attacks. The increased number of cases of malarial fevers is therefore accounted for.

On the other hand attacks, however mild, of the specific fevers, afford a certain protection. That this immunity applies to typhoid, as well as to yellow fever and to the eruptive fevers, there can be no doubt. Bartlett[1] especially dwells upon this point and advances evidence in favor of the truth of the assertion here made.

The history of armies in all parts of the world shows that new levies are especially subject to typhoid fever, and to the mild continued fevers so often called by some other name, while seasoned troops are to a large extent exempt from these diseases.

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[1] Elisha Bartlett, M.D.: The History, Diagnosis and Treatment of the Fevers of the United States, p. 98. Philadelphia, 1847.

There is good authority for the belief that malarial fevers have a tendency to disappear as countries become more populous and that they are superseded to a certain extent by enteric fevers. The causes of this diminished prevalence of malarial diseases in regions which have been long under cultivation we shall have occasion to refer to hereafter. The increased prevalence of enteric fevers is not difficult to account for; this, however, is a question outside of the scope of the present volume. But the inference, often made, that one class of fevers by a "change in type," has developed into the other, we must briefly refer to. We confess a general belief in evolution. We are convinced than the animal and vegetable organisms which existed during the earlier stages of the earth's history were of the simplest kind, and that those of the present day, however complex in organization, are the direct descendants of these early and simple forms. But when we see, as often happens, an indigenous plant displaced in a certain section of country by another plant of a different family, we do not infer that one has been evolved from the other. For example, since the buffalo has disappeared from the plains of Western Kansas, and settlements have gradually extended westward, the indigenous "buffalo-grass" is being supplanted by a grass of more vigorous growth, known locally as "blue-joint." West of a certain line the buffalo-grass occupies the territory, east of another line the blue-joint is almost the only native grass, while a broad margin between these lines is occupied by both, the buffalo-grass having the ascendency on the west and the blue-joint on the east, but the area of the former being constantly encroached upon by the latter. So as regards our two classes of fever. We are not satisfied that intermediate forms exist between periodic and enteric fevers; and when one class of fevers takes the place of another in a certain area we suspect that it is due to a substitution, resulting from changed conditions of soil, etc., of one morbific agent for another, rather than to a gradual transition of the pathogenic characters of the morbific agent which first occupied the ground. We admit, however, the difficulty of diagnosis when the effects of both poisons are manifested in the same individual.

MOUNTAIN FEVER.

Not having had personal opportunities for observing the so-called "mountain fever," we shall not attempt to give an extended account of this disease, which is by some supposed to be due to malaria, but submit the following quotations from three very competent observers, which seem to establish the fact that it is in truth a mild form of enteric fever.

Dr. Roberts Bartholow, when an Assistant Surgeon in the United States Army, had opportunities for studying this disease at Fort Bridger, Utah Territory. He says:

> Mountain fever is a term applied to a form of disease said to be peculiar to the elevated regions of the Rocky Mountains. . . . As already intimated, I consider typhoid fever as one of the forms of the so-called mountain fever. Two types of the affection are therefore to be described—the periodical and the continued. It will be seen farther on how these by certain local conditions are so much modified as to be readily confounded, and to present so many variations from the original type as to be considered an original disease. The periodical cases were usually remittents or quotidian intermittents. Many of the latter, when left to themselves, early assumed the

remittent type; consequently, remittent much more frequently came under treatment. . . . Two classes of cases occurred, differing only in intensity; the *mild* and the *grave*. The former, if left to the unassisted efforts of nature, after a variable duration, gradually ceased, but manifested a disposition to relapse at uncertain intervals; the latter, however, tended to the continued type, if not arrested by quinia, and were not easily distinguished from the typhoid cases, which, during the early stages, were unequivocally remittent. This is a fact with regard to the behavior of typhoid at considerable elevations, heretofore observed—the occurrence of distinct remissions, and it is this circumstance which, in my opinion, has confused the differential diagnosis of the two affections, creating the impression that they were forms of the same disease—"mountain fever."

The typhoid fever of Utah has other peculiarities besides the occurrence of remissions. Many of those general symptoms, so characteristic, were wanting—coma, subsultis tendinum, muttering delirium, floccitatio—but in all were present some mental disturbance and stupor, cophosis, epistaxis, gurgling on pressure over the ileocæcal valve, pea-green, watery stools; in two instances the "rose spots," and frequently the sudamina and sour-smelling perspirations. All the fatal cases were submitted to a post-mortem examination and the characteristic lesions of typhoid fever found.[1]

Assistant Surgeon W. N. Gardner, U.S.A., has also had opportunities for observing this so-called mountain fever. He says:

Typhoid fever is the great scourge of the Mexican towns; it occurs among the youth and young adults of both sexes, and is usually complicated with pneumonia. A form of this fever, not materially different from the well-recognized type, is frequently met with among mountaineers and miners, called mountain fever; in the only case in which I had an opportunity of making an autopsy, I found the usual lesions of typhoid.[2]

Assistant Surgeon Hoff, U.S.A., in a paper contributed to the *American Journal of the Medical Sciences* (January, 1880), arrives at the conclusion that the so-called "mountain fever" is a typho-malarial fever, or, in other words, typhoid fever in a malarial subject, or with a malarial complication. His conclusions are stated as follows:

1. The fever of the Rocky Mountain region is a hybrid disease, the prominent features of which are typhoid, the modifying intermittent; it is, in fact, the typho-malarial fever of Woodward.
2. It appears during or after exposure incident to field service, generally, though not necessarily, in late summer and early autumn, and seems to bear no relation to typhoid infection as now usually accepted by the profession.
3. At its inception this disease manifests itself as an intermittent of quotidian, tertian, or other form; this stage is followed (in about two weeks) by the typhoid stage, lasting in the neighborhood of four weeks, in which typical typhoid symptoms may be observed, modified to a greater or less degree by intermittent indications.
4. The pathological anatomy of the disease is that of typhoid fever.

Surgeon Charles Smart, U.S.A., has also studied this fever at Fort Bridger, U. T., and at Camp Douglass, Utah, and has contributed a valuable article to the literature of the subject.[3]

This author differs from those above quoted as to the character and etiology of the fever in question. According to him it is a "malarial remittent," and he believes it to result from the ingestion of "malarious waters," impregnated with malaria, not of local origin, but transported by the winds from distant localities, and washed from the higher strata of the atmosphere by falling snow and rain.

We cannot stop to discuss this theory of causation, but would remark that we greatly doubt the malarial origin of a fever having the characters given, which occurs in winter, and in a region where intermittents are not prevalent, even during the summer months. The peculiar characters of the disease as given by Dr. Smart are:

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[1] Am. J. M. Sc., Phila., April, 1860.

[2] Diseases Peculiar to Mountain Regions, Am. J. M. Sc., Phila., July, 1876.

[3] Am. J. M. Sc., Phila., January, 1878.

1. A primary stage of one, two, or more weeks, during which the individual is more or less oppressed by the influence of the *materies morbi*.
2. The development of fever, more or less marked, and more or less rapid in its course, with irregular remissions, and much more mental depression and muscular prostration than the patient's pulse and temperature would prepare the observer to find.
3. A typhoid stage, marked by prostration, emaciation, low delirium, and coma-vigil.

The present writer has seen numerous cases answering to this description at Fort Walla Walla, W. T., and has been disposed to attribute them to the use of contaminated drinking-water. But he does not believe that these cases of continued fever, which, as stated by Dr. Smart, often present "irregular remissions," are properly ascribed to the poison which produces typical intermittents and remittents, and which is known as malaria.

INFANTILE REMITTENT FEVER.

"This term has been applied to enteric fever as it occurs in children, for the reason that the pyrexia often assumes in them a distinctly remittent type throughout the whole course of the attack" (Wilson [1]).

"*The infantile remittent* of authors, so far as it is a distinct affection, is an example of simple irritative fever. Under that name, however, have been described several distinct diseases, resembling each other only in their febrile and remittent character, and in the circumstance of occurring in children. Gastritis, enteritis, mesenteric adenitis, hepatitis, tuberculous disease of the lungs and bowels, and *especially enteric or typhoid fever*, have been confounded under the vague title of infantile remittent" (Wood [2]).

MALARIAL DYSENTERY

The victims of chronic malarial poisoning are especially susceptible to attacks of diarrhœa and dysentery, when the special causes of these diseases prevail; and, on the other hand, an individual suffering from an alvine flux is more subject than one in perfect health to the action of the malarial poison. But that diarrhœa or dysentery are to be included among the direct manifestations of the action of malaria is very questionable. Diarrhœa and non-specific dysentery no doubt may occur as secondary results of malarial poisoning; but in this case it is not the malaria, but the local congestions and general debility of the digestive organs resulting from its continued action which gives rise to the flux; the immediate cause being, commonly, the presence of irritating material in the *primæ viæ* resulting from the imperfect digestion of food, or the presence of vitiated secretions.

That there is a specific dysentery, having a specific cause, is generally admitted by medical authorities; and, as in the case of enteric fever, this disease often occupies the same territory during its epidemic prevalence as that occupied by malarial fevers. Or it may exist as an endemic disease side by side with these fevers. The same general causes, heat, moisture, and organic matter undergoing decay, seem to be favorable to the production of the special malaria which produces dysentery as well as of that which produces intermittent fever. But it does not follow from this that the specific cause of the two forms of disease is the same.

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[1] The Continued Fevers, p. 195.

[2] Practice of Medicine, 5th ed., vol. i., p. 248.

Professor McLean, in his article on dysentery in Reynolds' "System of Medicine," says: "For my own part, I believe dysentery to be caused by the action on the blood of a poison having a peculiar affinity for the glandular structures of the large intestine. This poison I believe to be a malaria generated in the soil by the decomposition of organic matter."

Here the word malaria is evidently not used in its restricted signification, and we are ready to admit with Professor McLean that there is *a* malaria of dysentery. We believe also in *a* malaria of enteric fever, and in *a* malaria of yellow fever. But according to our view, these special kinds of malaria are essentially different from *the* malaria of intermittent fever, which is by common consent "malaria." The word is used in its restricted sense, as an adjective, in the article above referred to, where our author says: "In the *malarial form*, the course of the disease partakes of the periodic nature of the complication."

Professor Aitken is perhaps the strongest supporter of the view that dysentery and the malarial fevers are due to the same cause, and for the sake of stating fairly both sides of this question we quote from him quite fully.

> It may be stated as a general proposition that there is no country where paludal fever exists in which dysentery is not an endemic and prevailing disease. In the East and West Indies, in China, the Ionian Islands, Gibraltar, Malta, the Canadas, Holland, the coasts of Africa, as well as in many different parts of France, of the Peninsula, of the continent of America, and of the eastern parts of Great Britain, the prevalence of intermittent or remittent fevers and of dysentery is notorious.
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> This connection is so intimate that a given number of persons being exposed to the action of paludal miasmata, as, for example, a boat's crew sent ashore in a tropical climate, the probabilities are that of the men returning on board, part will be seized with dysentery and part with remittent fever.
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> Paludal fever and dysentery, moreover, are not only conjoined in locality, but they often coexist, precede, or follow each other in the same individual, so that the fever frequently ends in dysentery, and the dysentery in remittent fever. This proof of the common nature of these diseases is corroborated by every writer of any celebrity, and more especially by those who have detailed the diseases of our armies. But dysentery also prevails where there is no other evidence of the presence of malaria.[1]

We must confess that for us the last sentence in the above quotation has greater significance than all that precedes it. That malaria should be evolved in regions outside of the endemic prevalence of malarial diseases, in such amount as to produce serious and often fatal disease, and yet not manifest its presence by producing attacks of intermittent fever among those exposed to its influence, we cannot believe. But Professor Aitken remarks: "Nevertheless, the evidence in favor of malaria being the common, though probably not the sole cause of dysentery, appears to be so much the stronger." We can see no good reason for assuming that epidemic dysentery is due to a different cause when it occurs within or without the range of any particular endemic disease; and, as we have already remarked, we admit the probability that a non-specific dysentery may occur as a secondary result of malarial poisoning, and also from other causes quite independent of malaria.

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[1] Science and Practice of Medicine, vol. i., p. 581.

Following the course heretofore adopted in this INTRODUCTION of quoting freely from authorities rather than that of assuming to be an authority, we quote *in extenso* from Woodward[1] with reference to this point:

> The opinion that the poison, whatever it be, which causes the intermittent and remittent fevers is capable of acting upon the intestines under certain circumstances and of producing diarrhœa and dysentery has been expressed by many subsequent writers upon malaria and the malarial fevers, as for example, by Senac, Tournier, Bégin, Monfalcon, Macculloch, Mongellaz, Boudin, and Barker. Even those who, like Griesinger and Hertz, have been unwilling to commit themselves to this theory of causation, testify to the frequency with which dysentery and other fluxes occur in malarial regions, especially during the prevalence of the periodic fevers.
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> It would be easy to multiply examples of the epidemic and endemic occurrence of dysentery in association with intermittent and remittent fevers in various parts of Europe. . . . In tropical regions dysentery is not only more prevalent and more fatal than in temperate latitudes, but it is very much more frequently associated with the periodical fevers. It is, moreover, especially apt to prevail in those districts in which these fevers are endemic, and at the time of year when they are most frequent and fatal. These circumstances have not unnaturally led many physicians who have observed and described tropical diseases to embrace the opinion that the malaria which produces the fevers is also capable of giving rise to dysentery, and that a part at least of the tropical dysenteries are due to this cause. . . . But this view appears, after all, to have been based upon an incomplete view of the facts. While it is true that dysentery often prevails in malarial districts along with the malarial fevers, it is also true that it occurs where these fevers are almost or quite unknown, and that in some districts in which they are endemic dysentery is rare. . . .
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> Colin[2] has recently attempted to prove that it is the use for drinking purposes of the water, impregnated with decomposing organic matters, which is so often found in marshy regions, that causes the intestinal catarrhs and dysenteries which occur in these districts, while the malarial fevers are the result of aërial emanations. This suggestion, if true, would afford an explanation of many facts, especially in military experience, which are more difficult of explanation; but I am not satisfied that the argument by which it is supported does more than give it a certain air of probability as an ingenious hypothesis, and this hypothesis, it must be admitted, is hardly consistent with the facts to be presently brought forward with regard to the distribution of dysentery in time of peace mong the civil population of the United States. Nevertheless, it cannot be doubted that when the causes of dysentery act either upon a civil population or an army, those individuals whose resisting powers are diminished by debilitating constitutional conditions of any kind are especially prone to become victims, and in these cases the ordinary symptoms of dysentery are often complicated by phenomena resulting from the other morbid influences, whatever they may be. When the debilitating influence is malaria, whether expressed merely by the constitutional cachexia which may be described as chronic malarial poisoning, or by the actual existence of intermittent or remittent fevers, the ordinary course of dysentery is complicated by phenomena belonging to the malarial disease.
>
> During the war this complication was even more frequently observed than previously, because the great armies, moved suddenly from the Northern States into the malarial regions of the South, were exposed simultaneously to malarial influences and to the causes of dysentery. In the resulting compound, or hybrid forms of disease, the symptoms resulting from each cause often appeared together in the same individual from the beginning of the case to its end. Sometimes, however, dysentery, either by itself or as a sequel of diarrhœa, appeared as a primary disorder, assuming subsequently a periodic form, either as to the flux itself or as to the accompanying fever; or ague or remittent fever made its appearance during convalescence from dysentery, or after it had become chronic. In other cases the periodic fevers were the primary morbid condition, and dysentery alone, or preceded by diarrhœa, set in only after the health had been broken down by long-continued ague or after remittent fever had first been developed. Lastly, in yet other cases the malarial influence mani-

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[1] Medical and Surgical History of the War of the Rebellion, Part Second, Medical Volume.

[2] Ann. d'hyg., Par., xxxviii., 1872, p. 241.

fested itself by the production of chronic malarial poisoning; the resulting cachexia, whether existing by itself or associated with the mild scorbutic taint which was so widely spread among our troops, especially after the first year of the war, undoubtedly appeared to favor the development of dysentery as it did of diarrhœa. The subjects of this cachexia seemed less able to resist the causes of the disease than healthy men, and when once developed in them dysentery, even in its simple catarrhal forms, was more apt to become chronic and to prove fatal.

Having now passed in review certain forms of disease which we believe are improperly ascribed to malaria, we may proceed to inquire more particularly as regards the nature and effects of this morbific agent.

PART FIRST.

MALARIA.

Definition.—An unknown poison, of telluric origin, the cause of the periodic fevers.

We have seen in the Introduction to this volume that periodicity is not peculiar to malarial fevers. Nevertheless the periodic fevers, under which title we include the various types of intermittent and of remittent fever, are so well defined as a class and so widely known that there is no ambiguity in our definition.

A poison which is only known by its effects is necessarily a hypothetical substance, and there are not wanting those who deny altogether the existence of such an entity as malaria, and who would account for the disorders commonly ascribed to the action of this poison by the supposition that they are due to immaterial causes, such as refrigeration, electricity, etc.

We shall see as we proceed that this manner of accounting for the morbid phenomena known as intermittent and remittent fever is entirely insufficient and unsatisfactory, and that the general belief in a material agent as the cause of these phenomena has a most substantial foundation.

It would be idle to spend time in combating the various vagaries of medical philosophers who have attempted to account for the occurrence of these periodic fevers independently of the action of any material substance introduced into the body of the individual affected—*infected*. The modern belief that there is a material agent is indicated by the use of the term "infectious diseases," as applied to these and other diseases believed to be due to a specific cause, or infecting agent introduced from without.

Among the various attempts which have been made to account for the etiology of the periodic fevers upon a different hypothesis we may mention the following:

Hippocrates attributed tertians and quotidians to a superabundance of bile in the *primæ viæ*, and quotidians to atrabile. Galen referred quotidians to an alteration of the pituita, tertians to that of the bile, and quartans to putrescence of the atrabile. The atomists said that quartans were the result of an obstruction occasioned by the minutest atoms, tertians by those a little larger, and quotidians by the largest; Darwin attributed the phenomena of intermittence to the nutritive movement of composition and decomposition and the periodical recurrence of waking and sleep; Borelli, to an irritation of the nerves of the brain, and of the fibres of the heart, occasioned by an acidity or an acrimony developed in the nervous fluid; Werlhof referred it to the periodical movement of the earth; Mead and others attribute it to lunar influence and to the alternate action of day and night; Bailly endeavors to show that morbid intermittence is occasioned by the diurnal change in the position of the human body, from the upright to the recumbent position and the reverse (Maillot,[1] quoted from Bartlett).

According to Armand, the thermo- and electro-hygrometric phenomena of the atmosphere, by their combined action, their intensity and changeability, constitute the remote causes of fever, while the immediate causes lie in the changes produced in the entire organism, and especially in the nervous system, under these influences (Hertz).

Dr. Oldham,[2] of the Bengal Medical Service, has written a book to prove that malaria as a specific poison does not exist, but that the diseases attributed to it are produced by chill, or sudden abstraction of animal heat. According to his view, the extreme susceptibility to cold, which is caused by long-continued exposure to great heat, intensifies the predisposition to these diseases, thus causing their greater prevalence in hot climates. In cool climates, according to this theory, the powerfully chilling influence of damp is necessary for the development of the so-called malarial fevers. In such climates, accordingly, they rarely occur except in humid and marshy spots. Dr. Munro,[3] Deputy Surgeon-General of the English Army, claims priority in enunciating this view, having in a report published in 1862 said that he did not believe in the existence of malarious poison, but was convinced that fevers called malarious depended upon causes produced by rapid alterations of temperature acting upon the sympathetic nervous system.

The answer to all of these hypotheses is included in our definition. The cause of the periodic fevers—malaria—*is of telluric origin*. The evidence in favor of this assertion would fill volumes, and is beyond question. Those who go to sea in ships escape these fevers, in the latitudes where they prevail, until they approach the land. In tropical regions those who remain on board a vessel anchored at some distance from the shore remain in good health, while the boat-parties, sent ashore for provisions, etc., fall sick with *the fevers of the country*. We have African fevers, Panama fever, Bengal fever, etc., but who ever heard of Indian Ocean fevers, or Mediterranean fevers, or Gulf fevers? Any explanation, then, which attributes these fevers to general causes, the action of which is independent of locality, must be rejected.

And, for the same reason, we are unable to admit that changes originating within the human body can be the primary cause of these diseases. The explanations of Galen and of Hippocrates, however, are more tenable than those of the modern philosophers who ascribe malarial fevers to lunar influence, diurnal changes in the position of the human body, refrigeration, etc.; for we might admit such changes as they refer to, in the fluids which find their way into the *primæ viæ*, as immediate or secondary causes, induced by a primary cause from without—the telluric poison which we call malaria.

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[1] Traité des Fièvres Intermittentes.

[2] C. F. Oldham, M.R.C.P.E., etc.: What is Malaria? London, 1871.

[3] Remarks upon Malarious Fevers, etc. Report English Army Medical Department, 1872, Appendix, p. 266.

CHAPTER I.

MODE OF INFECTION, OR INTOXICATION (?).

The malarial diseases are included by Liebermeister in his group of "Infectious Diseases," which, according to his definition, originate through the infection of the system with certain peculiar poisonous matters, which are mainly distinguished from the ordinary poisons by the fact that they can reproduce themselves under favoring conditions to an endless degree. They also fall within the sub-group of "miasmatic infectious diseases," in which the poison *develops itself* externally; its reception into a higher organism not being necessary to its reproduction.[1]

Now to admit that the malarial poison reproduces itself external to the body would be to concede, at the outset, that it is a living germ. This we are not prepared to do, and consequently place at the head of this chapter, "Mode of Infection or Intoxication (?)."

There can be no question as to the manner in which malarial poisoning usually occurs. The term *malaria* indicates the usual belief that it is due to contamination of the atmosphere—bad air; and a multitude of facts support this belief. A brief exposure in such a contaminated atmosphere, in intensely malarious regions, is often sufficient to produce poisoning of the most serious character; and it is well established that in such regions the atmosphere is more highly charged with malaria at night than during the daytime; that the poison is more intense near the ground than at a little elevation above the surface from which it is evolved; that it may be carried by the winds from the locality where it is produced, etc.

The fact that poisoning, in any disease, results from the respiration of an infected atmosphere cannot, however, be taken as evidence that the poison is not particulate, or that it effects an entrance by way of the lungs. The air is, to a certain extent, purified of the floating particles suspended in it before it reaches the lungs, by the deposition of these particles upon the moist mucous membrane of the anterior and posterior nares, which seems to be especially adapted for this purpose. When these particles are comparatively large and dark-colored, we may easily have ocular evidence of the efficiency of this apparatus for purifying the air before it passes to the lungs. As, for example, when one uses a pocket-handkerchief after having respired, for a short time, an atmosphere charged with minute particles of carbon-smoke. Particles of all kinds arrested in this manner find their way, in part at least, to the stomach, and there can be little doubt that disease-germs contained in the atmosphere might thus gain access to the intestine.

The possibility of the absorption of the malarial poison through the skin cannot be denied, but we have no evidence relating to this mode of infection, which at all events must be of trifling importance as compared with the effects of respiring a malarious atmosphere.

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[1] Introduction to Ziemssen's Cyclopædia, American edition, vol. i.

The question whether malarial poisoning may result from the drinking of surface-water in malarious regions is one of great importance, and one which of late years has received considerable attention.

It is well-established that enteric fever and certain alvine fluxes may result from the use of contaminated drinking-water. And in the case of the former disease we know that even very great dilution does not destroy the infectious properties of the contaminated water; *e.g.*, in those cases where it has been used to wash vessels in which milk was placed, and in which typhoid fever has resulted from drinking this.

That fevers having an intermittent or remittent character may also be produced in the same way cannot be doubted. But we have already seen, in the Introduction to the present volume, that enteric fever frequently presents these characters; that in this case the differential diagnosis from malarial fevers presents great difficulties; and that in many parts of the world fevers of this character are attributed, without question, to malaria. We therefore feel inclined to accept the evidence with a great deal of caution. Moreover, we think that considerable weight should be accorded to the negative evidence. It would seem that if this mode of infection occurs at all, it should occur frequently, and in that case that it would be more generally recognized. From what has been said in the Introduction, it will be seen that we cannot accept evidence relating to the production of "malarial diarrhœa," or "malarial dysentery," or "mountain fever," or "continued remittent fever," or "typho-malarial fever" in any of its forms.

If malarial diseases are produced at all by the ingestion of "malarious waters" we have reason to expect that typical intermittents will be so produced. And as there may be some question as to the etiology of continued or pernicious remittents, we are justified in demanding that these be excluded in the consideration of this question.

Dr. Parkes was the strongest advocate of the view that malarial fevers may result in the way indicated. His opinion is entitled to the greatest consideration. But we would remark that the facts adduced in support of this opinion did not come under his personal observation and are in great part drawn from the reports of English physicians practising in India, where, as he himself says: "At the present time in India the opinion seems to be gaining ground that the prevalent notions about malaria require to be reconsidered; that 'malaria' is much less common than is supposed, and that the mixing up of relapsing fever, typhoid fever, and perhaps other specific fevers with malarious diseases has caused so much confusion that all old observations should be thrown aside."[1]

Much of the evidence presented by Parkes in his "Practical Hygiene" is so vague as to the nature of the fever produced by drinking surface-water that we can accord it but little weight. Thus, we read that "it has been a very general belief among the inhabitants of marshy countries that the water could produce fever."

"Henry Marshall says that the Singhalese attribute fevers to impure water, especially if elephants or buffaloes have been washing in it, and it is to be presumed that he referred to periodical fevers."

"It is stated by Mr. Bettington, of the Madras Civil Service, that it is notorious that the water produces fever and affections of the spleen. The essay by this gentleman gives, indeed, some extremely strong evidence on this point. He refers to villages placed under the same conditions as to marsh air, but in some of which *fevers* are prevalent, in others not; the only difference is, that the latter are supplied with pure water, the former with marsh- or nullah-water full of vegetable débris."

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[1] Report English Army Medical Department, 1870, Appendix, p. 239.

"Another village (Tambatz) was also 'notoriously unhealthy;' a well was dug and the inhabitants became healthy."

"At Sheerness the use of the ditch-water, which is highly impure with vegetable débris, has been also considered to be one of the chief causes of the extraordinary insalubrity."[1]

Cases of this kind might be multiplied indefinitely. It is generally admitted that a contaminated water-supply is a common cause of insalubrity. Colin has suggested that when intermittent fever prevails more extensively among those who drink impure water, than among others similarly situated who use pure water, it may be the result, simply, of greater susceptibility to the influence of the malarial poison present in the air among those whose health has been affected by the use of impure water.

With his usual fairness Parkes quotes the opinion of the author last referred to, as follows:

"Professor Colin, of the Val de Grace, who is so well known for his researches on intermittent fever, is also inclined to question the production of paroxysmal fevers by marsh-water. He cites numerous cases in Algiers and Italy, where impure marsh-water gave rise to indigestion, diarrhœa, and dysentery, but in no case to intermittent fever, and in all his observations he had never met with an instance of such an origin of ague."

That a *pernicious septic* fever may result in rabbits from the introduction beneath their skin of water contaminated with organic matter and septic organisms, is shown by the following experiments made by the writer in New Orleans during the summer of 1880:[2]

Experiment No. 13.

Rabbit No. 12.—October 7th, 9 A.M., injected into right flank 1.35 c.c. of water shaken up with a little material scraped from the surface of gutter-mud in front of my laboratory (corner of Gravier and Rampart Streets, New Orleans). 1 P.M., temperature 106°; 6 P.M., 107°. October 9th, 8.30 A.M., 106°; 1 P.M., 106°; 6 P.M., 109°. October 10th, 9. A.M., found dead. Post-mortem examination shows diffuse cellulitis and gangrenous sloughing of the integument and subjacent tissues of the right side of the belly. So extensive has been this sloughing that the intestines are exposed. A very offensive odor of putrefaction is given off from the gangrenous tissues. The rabbit must have died early in the night, and was so offensive that no further examination was made.

Experiment No. 20.

Rabbit No. 18.—October 18th, injected into cellular tissue 2 c.c. of water to which had been added, October 10th, surface mud from artificial marsh No. 2. This had been shaken up in a test-tube and then allowed to stand until the date of the injection. Temperature: 1.30 P.M., 104°; 6 P.M., 103.5°. October 19th, 8.30 A.M., 105°; 1 P.M., 106°; 5.30 P.M., 106°. October 20th, 8.30 A.M., 100.6°; 1 P.M., dead. Post-mortem examination immediately. Diffuse cellulitis extending from point of injection. Bloody serum from cellular tissue swarms with bacteria (*B. termo*, bacilli, micrococci). Liver weighs 534 grains, congested. No organisms recognized in scrapings from freshly cut surface of liver, in blood from heart, or in spleen pulp. Liver contains much fat.

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[1] Practical Hygiene, 5th ed., p. 44.

[2] Supplement No. 14, National Board of Health Bulletin. Washington, July 23, 1881.

Experiment No. 34.

Rabbit No. 19.—A full-grown male. November 18th, 11 A.M., injected 1.26 c.c. of water shaken up with surface slime scraped from the gutter-mud in front of laboratory. 5.30 P.M., temperature 105°. November 19th, 8.30 A.M., 105.2°; 2.30 P.M., 105°; November 20th, 8.30 A.M., 103.5°; November 21st, 10 A.M., 103.5°; November 22d, 8.30 A.M., rabbit found dead. Post-mortem examination shows diffuse cellulitis extending from point of injection, with effusion of bloody serum, which swarms with bacteria.

That the ingestion of water contaminated in the same way would also have produced fever in these rabbits the writer is not prepared to affirm, not having made the experiment. But that the drinking of such water by man is often followed by the most serious consequences is incontestible.

The case of the Argo, recorded by Boudin, is cited by Parkes as "an extremely strong one." Chaumont remarks in regard to this case: "The evidence seemed very strong until contested by Colin."[1]

We give Colin's account of the case, as it is fuller than that of Parkes, and because we fully agree with the criticisms made by this author.

> In the month of July, 1837, the ship Argo sailed fron Bône with 120 healthy soldiers on board. During the short journey to Marseilles 13 men died and were thrown into the sea; and upon the arrival of the vessel 98 men were placed in the hospital of the lazaretto at Marseilles, offering the most decided signs of malarial intoxication in all its forms and types. While the soldiers were attacked with fevers, choleraic, epileptic, comatose, tetanic, etc., which yielded as by enchantment to sulphate of quinine in full doses, the crew of the ship remained in perfect health. The only difference revealed by a searching inquiry related to the water-supply of the sailors and soldiers. The former had a separate and pure provision of water for drinking; the latter were supplied with water obtained in the vicinity of Bône from a marshy place, and embarked in haste. Some soldiers escaped who were able to purchase, from their savings, water from the sailors.

M. Colin criticises this case as follows:

"Notwithstanding the great authority of Boudin, this account has always inspired me with more astonishment than conviction. It is a fact without analogy in the history of intermittent fevers. Has any one ever seen an example of like gravity of an epidemic of malarial origin in the latitude of the Mediterranean, and in the short space of a journey between Algeria and France? It is a figure far in excess of the mortality of our army in Africa, where the individuals are subject to intoxication not only from drinking impure water, but by way of the pulmonary and cutaneous surfaces as well."[2]

From another account of this epidemic, written by Léonard, M. Colin arrives at the conclusion that the disease in this case was enteric fever. We would suggest that the violence of the symptoms and rapidly fatal character of the disease rather indicate non-specific septic poisoning. In this case the benefit which is said to have resulted from the liberal use of quinine would not be surprising; whereas in enteric fever, the continuance of which depends upon the existence of a local lesion, quinine does not arrest the progress of the disease.

In the *Virginia Medical Monthly* of December, 1874, Dr. Herbert Nash asserts that in the vicinity of Norfolk, Va., families which previously suffered from malarial fevers escaped after discontinuing the use of spring- and well-waters and using that from cisterns only.

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[1] Rev. d'hyg., Par., 1879, p. 101.

[2] De l'ingestion des eaux marécageuses comme cause de la dysentérie et des fièvres intermittentes. Paris, 1872.

This statement is quite as definite and as worthy of confidence as many of the examples cited by Parkes. But in a later number of the same journal we find it contradicted by another physician, Dr. Tebault, practising in the same county, who says that the well- and spring-waters in question produce gastro-enteric symptoms, but not paludal fevers. This case is cited simply to show how intimately the question of etiology is associated with that of diagnosis, and how necessary it is to be cautious as regards the evidence in considering a question of this kind.

The author recently had related to him by a medical officer of the army, the facts relating to the prevalence of intermittent fevers at an army post in Arizona. A very notable decrease in the number of cases was observed after the command discontinued the use, for drinking purposes, of the water of a small stream, which, during a portion of its course, was hidden in its sandy bed, and which no doubt contained a considerable amount of organic impurities. The case seemed a very strong one, but the evidence lost much of its value when it was ascertained that not only had a pure water supply been obtained by sinking wells, but the command had been moved, some time before the wells were dug, from the banks of the stream to the top of the high "mesa" through which its channel had been eroded. This case is introduced simply to show that essential factors are often overlooked by those who furnish the data upon which theories of one kind or another are founded.

These remarks are made in the interest of conservatism and truth and not for the purpose of combating a view which has much in its favor, and which is worthy of the fullest investigation. In a recent work[1] by Dr. Russell, of the Bengal Medical Service, this view is supported in a most positive manner. The facts given are for the most part drawn from Parkes' "Hygiene," and have already been referred to. The author states the results of his personal observations as follows:

> The writer's personal and professional experience during seven years in one of the most intense malaria-producing regions in India has convinced him of the marked immunity from malarial affections enjoyed by persons who, though living continuously in this typically malarious region, yet carefully avoid introducing the miasm into their systems in their drinking-water. Among the ordinary populations, who habitually drink raw water, directly or indirectly of marsh origin, malarial affections of one kind or other may be said to be almost universal.
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> Among the Europeans and enlightened natives, who have of late years paid more attention to their supply of drinking-water, malarial affections have markedly decreased in frequency and severity.
>
> Those who habitually avoid the use of water directly or indirectly of swamp origin, and who take care to destroy the germs of malaria (by boiling and filtering their water or making it into tea), enjoy, even in these intensely moist, malarial regions, abounding in jungle and marsh, an immunity from diseases of malarial origin nearly equal to that enjoyed by residents of non-malarious tropical climates. . . .
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> The following instance has occurred in the writer's own experience:
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> The journey from the plains to the hill-station of Assam commences at Ganhati (180 feet above the sea-level) and terminates at the station of Shillong, in the Khasia hills (4,600 feet high). This journey of sixty-four miles is usually broken by a halt, for one night, at the mid-way Dâk bungalow of Nungpho (1,300 feet high). So frequently was an attack of fever acquired during this single night's halt that such an attack used to be looked on as a necessary and almost unavoidable accompaniment of the journey. Quinine was invariably taken on the journey as an essential prophylactic, and the approved and generally adopted custom was that the traveller should at

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[1] Malaria, its Cause and Effects. London, 1880.

> sunset shut himself almost hermetically in his bedroom beneath the mosquito-curtains, and, if possible, beneath the bedclothes.
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> It was held that the miasm was carried up the ravine by currents of air from the malarial plains and concentrated in the narrow valley in which Nungpho is situated. Practically, however, the currents of cool air are found to set down these elevated valleys to the plains below, to supply the rarefied currents of heated air which ascend from the hot plains to the higher regions of the atmosphere.
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> The malaria of Nungpho is now admitted to be of local origin, and its mode of introduction into the system is tolerably well ascertained to be through the water supply. The only water procurable at Nungpho is that of extensive swampy tracts, or of small streams entirely derived from the drainage of contiguous terais, swamps, and paddy-lands, in which are concentrated all the elements of malaria. So clearly is this now understood that the traveller of the present day absolutely avoids all use of the local water at that station, and usually travels furnished with supplies of pure liquids, or drinks no water on the journey. It is now common to find the traveller at Nungpho armed with a bottle of pure water or tea, brought with him; and even more faith is put in this than in the prophylactic use of quinine. It is certain that now attacks of fever rarely result from this journey; and Nungpho has almost died out of memory as a fever-producing region so far as Europeans are concerned. Natives, however, suffer almost as frequently as formerly, and a night at that station is still dreaded by them as a harbinger of an attack of ague. The reason, no doubt, is that they use the most convenient and indeed the only water accessible, viz., the drainage of the terais saturated with water.

In our own country numerous observations have been recorded which seem to connect the prevalence of malarial diseases with the drinking of surface-water obtained from shallow wells. But it must be remembered that the fact that the wells are shallow is evidence that the ground-water in that vicinity is near the surface. We shall see later that stagnant ground-water is one of the most potent factors concerned in the evolution of malaria from the soil; and we have ample evidence that malarial fevers may be contracted where this and other necessary factors for the production of malaria are present, independently of the drinking of surface-water.

It is evident, then, that the fact that in a certain section the inhabitants drink water from shallow wells and suffer from intermittent fever has no great value in establishing this mode of infection, unless it can be shown that in the same section those who abstain from drinking this surface-water escape.

The following interesting statement from a careful observer shows very well the general fact that malarial fevers are more prevalent where the ground-water is near the surface, but the gentleman who records the observations is careful to say: "Whether it is due to the mere presence or to the fact that it is drunk, or to both, I am unable to say."

> Some years ago, while engaged in the study of irrigation—then beginning to be applied on the dry plains of California—I was led to notice the level of standing water in wells, in reference to which there is a great difference in our interior plains. I soon noticed that shallow wells and malaria were frequent companions. Where the wells were seventy feet, or thereabouts, deep, there was freedom from malaria. Having noticed these coincidences, I afterward investigated their occurrence in a great many cases by inquiries of farmers with whom I had conversation. In one or two cases of exceptional malarial districts in the foot-hills, which are generally free from this pest, I found the water in the wells near the surface. I do not recall a single instance of shallow wells where the family were free from fevers, always intermittent, I believe. I therefore connected the presence of water near the surface of the ground with the existence of malaria. Whether it is due to the mere presence or to the fact that it is drunk, or to both, I am unable to say.[1]

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[1] Extract from letter to the present writer from Col. George H. Mendel, of the Engineer Corps, U.S.A., dated San Francisco, Cal., Feb. 10, 1883.

Some of the recorded observations are more definite as to the relation of attacks of intermittent fever to the ingestion of surface-water. Our space does not permit an extended reproduction of these observations, but we quote the following as apparently quite definite in support of the affirmative answer to this question. Our conservatism induces us, however, to remark that quite as definite observations have been recorded in favor of transmission by personal contact, and that we do not consider the question by any means definitely settled.

> Mr. Blower, of Bedford, England, mentions a case in which, in the parish of Houghton, almost the only family which escaped ague, at one time, was that of a farmer who used well-water, while all the other inhabitants drank ditch-water.[1]

Dr. Thomas W. Hervey, in an interesting paper relating to malaria, gives some valuable details with reference to the prevalence of intermittent fever in the vicinity of Orange, N. J. We quote from his paper the following:

> I will repeat, then, that in this small area, where we find as conditions a saturated subsoil and other recognized factors for the production of malaria, where the use of shallow wells is almost universal, and where we find the surrounding, better-drained localities free from disease, here, I say, we find that ninety per cent. of the families are afflicted with effects of malaria.
>
> One of the exceptions, Mr. H——, an intelligent New York lawyer, told me that while he used the well on his place his family were always sick with the chills. Since using cistern-water for the last three years they have been entirely free from the disease. This case is similar to one reported to the *Medical and Surgical Reporter* from Virginia, where in a certain valley where intermittents prevailed it was noticed that the old settlers who used the wells were the victims, and the new-comers who used water supplied from cisterns escaped.
>
> The use of cistern-water is not at all prevalent in Orange, nor can I find another family who use it for drinking-water in the district we are studying. This is the only family that I am sure has escaped fever and ague during my observations.
>
> Another family were the victims of the disease every year for certainly three years. During the last eighteen months, though visited by other diseases, they have had no ague in the house. During this period they have ceased to use their old shallow well, and use a driven well some sixty feet deep, entering the rock about thirty feet. This has been the longest time that they have ever been free from the disease.
>
> At the lowest point of the road where it crosses the brook there are several houses where these diseases are never absent, except occasionally in the depths of winter. Seven families take their drinking-water from a shallow well situated but thirty feet from the brook. The house that is constantly supplied from this well is never free from the disease. Family after family occupy it, and in every instance every person will have the chills. People move to it who have never had the ague, and who perhaps have lived in this neighborhood and escaped hitherto, and soon they will be down with the disease. They will move half a mile away and never have any more of it.[2]

Our author adds: "These are not proofs, you will say; they might receive the disease through the lungs nevertheless." This element of uncertainty applies to most of the cases which have been advanced in support of the view that infection has occurred through drinking-water. In the instance last mentioned the houses where the disease is never absent except in the depths of winter, are *at the lowest point of the road where it crosses the brook, and a move of half a mile* from the house which has the worst reputation gave immunity. If the water from the shallow well at the house where everybody had ague, could be given regularly for some time to persons living outside of the malarial district, we would have a crucial experiment, the results of which would be sufficiently convincing to satisfy the demands of science; but in the absence of such experimental proof we must still preserve our scientific skepticism, although, as heretofore stated, we admit that there is much evidence which appears strongly to sustain the view that malarial infection may occur as the result of the ingestion of "malarious waters."

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[1] Youman's Huxley, par. 415, p. 380, N. Y. ed., 1881.

[2] The Sanitary News, Feb. 1, 1884.

CONTAGION.—The general verdict of the profession is opposed to the belief that fevers strictly malarial in their origin may be communicated by personal contact. But there are not wanting authors who favor this view. Béringuier[1] especially has given a series of examples which have convinced him of the possibility of this mode of infection, which, he says, he was not at first willing to believe. The twelve examples given all relate to cases in which healthy persons, not otherwise exposed, have been seized with ague after sleeping in the same bed with one subject to attacks, during the sweating stage of a paroxysm. We quote a single case only:

> Madam V—— passed the autumn in the country, and contracted there intermittent fever which was arrested by the use of quinine. In November she returned to the city, and fifteen days after she was unexpectedly seized during the night with a return of the disease; soon she was in a profuse perspiration; her husband remained in bed with her during the attack. Three days later he was seized with a chill which proved to be the first access of a tertian intermittent.

We may remark that the cases reported by Béringuier, in support of communication by personal contact, are quite as definite and well attested as those above given in favor of the view that infection may occur through drinking-water, or that malaria may be evolved from piles of decomposing vegetable material, *e.g.*, from *Optunia vulgaris* in a state of decomposition (see p. 51).

It has also been claimed that a nursing infant may contract malarial fever through the milk of its mother or wet-nurse. "Boxa declares that in Pola ninety per cent. of the children suckled by mothers or nurses with malarial fever were attacked with the disease" (Hertz). It is hardly necessary to remark that the mothers and their infants being subject to the same external conditions, it seems more probable that both contracted the disease in the same way rather than that the infant contracted ague in this indirect manner.

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[1] Traité des Fièvres Intermittentes et Remittentes. Paris, 1865.

CHAPTER II.

CONDITIONS GOVERNING THE EVOLUTION AND DISSEMINATION OF MALARIA.

THE malarial poison is of telluric origin, but its production, as manifested by its effects, is limited to certain parts of the earth's surface, and is governed by conditions relating to soil, climate, and topography, which will receive consideration in the present section.

CONDITIONS RELATING TO SOIL AND TO VEGETATION.

Malaria, although indisputably of telluric origin, is not given off from every kind of earth. Those who mould clay into bricks or earthen-ware, and those who excavate banks of pure sand or gravel, are not subject to attacks of malarial fevers by reason of their occupation. On the other hand, agricultural laborers who are exposed to the emanations from a soil rich in organic material are especially liable to be attacked by these fevers.

The evidence connecting the production of malaria with the presence of organic matter in the soil is overwhelming and conclusive. But it does not follow that a considerable amount of organic matter is essential. No doubt in rich virgin soils the amount is very much in excess of that required for the abundant evolution of malaria, for it is only after being cultivated for a series of years that the malarious emanations from such soils are perceptibly diminished. And, on the other hand, there is ample evidence that sandy soils containing comparatively little organic matter may produce malaria. The general rule, however, holds good that soils rich in organic matter are most prolific of malaria. Such soils are found in low, marshy places, in the deltas of great rivers, in the broad alluvial plains bordering great rivers, and in the valleys of smaller streams.

The geological character of the soil, as pointed out by Colin, is not an essential condition, for malarial fevers may prevail in regions having a surface soil of the most varied composition—calcareous, sandy, argillaceous, or even granitic.

An impervious subsoil, of whatever character, is everywhere recognized as a condition favorable for the production of malaria, and this presumably because it retains water, which, as we shall see, is an essential factor.

The intimate association in many parts of the world of malarial fevers with marshes has given rise to the designation paludal or marsh fevers, as applied to these diseases, and malaria is very commonly spoken of as a paludal miasm, or as the marsh poison. These terms have been objected to on the ground that malarial fevers occur as well in non-marshy localities. But the general fact must be admitted that a certain amount of moisture in the soil is essential for the production of malaria, and that malarial fevers are more prevalent and more severe in low, marshy localities than in elevated, well-drained lands.

When the surface is rendered impervious by desiccation, as in countries having little rainfall, and in which the soil is of such a character as to "bake" under the influence of the solar rays, malaria is not evolved to any considerable extent, although there may be sufficient moisture beneath the surface to sustain more or less vegetation. It is probable that in this case the development of malaria is prevented by the exclusion of air from the soil, for many circumstances make it appear probable that the presence of oxygen is an essential condition. It is apparently for this reason that malaria is given off from a porous, sandy soil, especially when there is an impervious subsoil, more freely than from a stiff soil which "bakes," although the latter may contain a larger amount of organic material.

The covering of the surface by water effectually prevents the evolution of malaria. The same is true, to a great extent, as regards a surface covered by forest trees, or by dense vegetation of any kind. Here the exclusion of oxygen is probably but one of several causes which come into play to produce the result stated. Among these we may mention the protection of the surface from the direct rays of the sun, the consumption by the growing vegetation of materials in the soil required for the production of malaria, and perhaps its absorption, after being set free from the soil, by the green parts of growing plants. All of these agencies, to a great extent, cease to act in the autumn, when deciduous plants shed their leaves and vegetation generally is at a standstill. This would seem to be the cause of the increased prevalence of malarial fevers, commonly observed at this season, rather than the usually assigned cause, viz., the addition to the organic material in the soil of the annual crop of leaves, etc. These require time for their decomposition, and there is reason to believe that any soil which is capable of producing such a crop contains, without this addition, an ample quantity of organic material for the abundant development of malaria.

We shall now consider more in detail the facts relating to the soil and to vegetation, as influencing the production of malaria.

MARSHES.—M. Colin, accepting the definition of a marsh given by Parent-Duchâtelet,[1] says: "For us, as for all actual observers, the marsh constitutes the most efficient condition for the development of the affections under consideration."

It is generally conceded that there are, in various parts of the world, non-malarious marshes. But it is probable that a considerable number of these would not come within the definition of Parent-Duchâtelet, an essential condition being that the surface is only submerged during a part of the year.

All observers agree that it is when the surface of such a marsh is exposed that malarious exhalations are given off, and that when completely covered with water it is, like a pond or lake, innocuous. Sir Joseph Fayrer states that in India "malaria is at its worst during the drying-up season, after the rains and the beginning of the cold season. In the dry, hot weather, and during the heavy rains, *when the ground is covered with water*, or when the land has been for some time cultivated and populated, or covered with trees or even fresh turf, it is less severe."[2]

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[1] On appelle *marais*, dit Parent-Duchâtelet, une surface submergée pendant une partie de l'année, s'humectant et se desséchant alternativement.—*Traité des Fièvres Intermittentes*, p. 2. Paris, 1870.

[2] Climate and Fevers of India, p. 42.

The deleterious effects of marshes may doubtless be neutralized to a great extent by currents of air, as when they are situated upon low islands within the influence of the "trade-winds." The Bermudas furnish a good example of this. Marshy spots are not infrequent upon these islands, but all observers agree that intermittent fever of endemic origin is unknown. This has been ascribed to the fact that the trees and plants are not deciduous, and that consequently there is but little vegetable decomposition. The influence of the sea-winds which sweep these islands constantly is, however, in all probability the most important cause of this exemption.

Hertz [1] suggests that the disinfecting properties of ozone, which is said to be developed largely in some marshes, may account for the instances where "with every condition present for the development of malaria this poison is entirely lacking." According to Parkes,[2] peaty soils and those which are regularly overflowed by the sea do not produce malaria.

It is well known that some salt marshes give off an extremely noxious malaria, while others, even in tropical latitudes, are quite harmless. Thus Hertz says: "Marshes that are formed partly of salt water, especially delta lands, are far more noxious than those supplied entirely with fresh water. This is believed to be due to the action of salt water in killing fresh-water plants and thus producing a larger amount of decomposing material."[3] This explanation may apply to marshes subjected to occasional overflow, while the statement of Parkes that those marshes subject to daily overflow by the tides do not produce malaria is probably the true explanation of the apparent exceptions which have been recorded by travellers.

The analyses of the worst malarious marshes show a large amount of vegetable organic matter. A marsh in Trinidad gave thirty-five per cent.; the middle layer in the Tuscan Maremma thirty per cent. The organic matter is made up of humic, ulmic, crenic, and apocrenic acids—all substances which require renewed investigation at the hands of chemists. Vegetable matter embedded in the soil decomposes very slowly; in the Tuscan Maremma, which must have existed many centuries, if not thousands of years, many of the plants are still undestroyed.[4]

The disappearance of malarial fevers as a result of the drainage and cultivation of marshes has been repeatedly observed. Hirsch has given instances of this,[5] and the literature of the subject abounds in examples. This is well illustrated by the results of drainage and improved cultivation in parts of England, and notably in Lincolnshire, where the "fens" were formerly a prolific source of malaria.

Malarious Plains.—By far the largest proportion of cases of malarial fevers originate, not from exposure to the air of marshes, but from the malaria given off from damp bottom-lands, from the deltas of rivers subject to annual overflow, from the margins of streams when these are exposed during the dry season, and especially from alluvial plains under cultivation. This naturally results from the necessary exposure in these situations, and from the fact that malarious marshes are avoided as far as possible. But it is not alone the low alluvial plains which produce malaria. Elevated mountain valleys and sandy plains, in some instances, are noted for the prevalence of malarial fevers.

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[1] Ziemssen's Cyclopædia, vol. i., p. 564.
[2] Practical Hygiene, 5th ed., p. 342.
[3] Ziemssen's Cyclopædia, vol. i., p. 564.
[4] Parkes: Practical Hygiene, p. 342.
[5] Handbuch der Historisch-geographischen Pathologie, p. 52, note.

Sandy plains, when there is an impervious substratum of any kind, are, perhaps, more prolific sources of malaria than undisturbed alluvium, especially when the surface of this is baked by the sun, or covered with vegetation. But when the latter is disturbed by the plow of the farmer, or in the prosecution of engineering operations, the case is reversed. The superabundance of organic material in the soil, which was previously, so to speak, a latent factor, now comes into play; and the atmosphere having free access to this material—in the presence of sufficient heat and moisture —malaria is abundantly, and we may almost say universally, produced. This is a matter of such common observation in our own country that it seems hardly necessary to dwell upon it. Even the plains of Central Kansas, which are high and dry, where a few years since the buffalo and the nomadic Indian had undisputed possession, give off malaria when the virgin soil is turned up by the plow of the settler.

The conditions relating to the Roman Campagna are especially interesting and instructive, as this plain has a world-wide reputation as a fertile source of malaria. According to Tommasi-Crudeli the superficial layer containing organic material of vegetable origin is of little thickness. Beneath this is a layer of sand or of débris of lava; and below this an argillaceous subsoil, which retains the water and forms underground collections in depressed localities. These collections are not only supplied by the rain-water, but also from ponds situated at higher levels.

M. Colin devotes ninety pages of his work[1] to a "special study of the influences which contribute to the development of malaria in the Roman Campagna." The limits of the present volume will not permit us to quote extensively from this valuable contribution to the etiology of malaria, but we give below a *résumé* of the results reached.

> To sum up, in the Roman Campagna malaria is produced everywhere, and has no specially limited foci, marshy or otherwise.
>
> It draws its origin from the richness of a soil formerly covered with forests or with cultivated fields, which have to-day been replaced by grazing grounds insufficient to exhaust the vegetative potency of the soil.
>
> Heat is indispensable to the development of telluric fevers: it modifies the type, accelerates the explosion, but by itself is insufficient to produce them.
>
> The reappearance of malaria throughout the entire extent of the Campagna explains the insalubrity of Rome at all points of its circumference.
>
> The regions which enjoy the most complete immunity are those where the population is most dense.

According to M. Colin the atmosphere obtains access and the malarial exhalations escape from the soil of the campagna during the dry season, after the month of June, from numerous fissures in the baked surface, which to a considerable extent take the place of the spade of the laborer in cultivated regions.

In India malarial fevers are especially prevalent in the terai, "which is a belt of low, swampy, forest ground at the foot of the Himalaya Mountains, where the porous soil has a substratum of clay by which the water is brought and retained near the surface. . . . It is scarcely less active on high and arid sandy ground, as in the Deccan, Sind, Bicaneer, Peshawur, the Punjab, Bhawulpore; but even in these localities subsoil, damp, and organic matter—for there is always some—appear to be at the bottom of it. . . . The low-lying, swampy ground of the Concan, and the dry, arid, sandy plains of Marwar, are contrasted by Moore; they are very different, yet malarious fever prevails equally on both."[1]

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[1] Traité des Fièvres Intermittentes, Art. II.

Soil Moisture.—From what has already been said, it is evident that a certain amount of moisture in the soil is essential for the evolution of malaria. All authorities agree upon this. Even in the dryest regions the soil contains more or less moisture coming from below, and often there is a subterranean sheet of water, at no great depth, in regions where the rainfall is extremely light. The oases of the desert of Sahara, according to Hirsch, are produced by trough-like depressions or excavations in a rocky bed, which serve as a receptacle for subterranean waters, and here malarial fevers may prevail. The development of malaria may be connected either with rise or with fall of the ground-water (Parkes). An impeded outflow, resulting from interference with the natural or artificial drainage of a malarious region, is especially dangerous. Fayrer says that Indian experience fully supports the view, long since expressed by Pringle, that the chief determining cause of malaria is *stagnant subsoil water*. Numerous illustrations of this fact are to be found in the United States; and, in general, it may be said that an impervious subsoil, especially when it presents depressions which prevent the natural movement of the ground-water, covered by a porous surface soil, furnishes conditions most favorable for the development of malaria.

Ground-air.—The presence of ground-air seems to be quite as important a factor as that of ground-water, for, as we have seen, it is more especially porous soils which give off malaria when undisturbed, while compact soils are comparatively innocuous until they are exposed to the air by the interference of man. This fact is further illustrated by the results which follow the exclusion of air from the soil of a previously malarious locality by the building up of a city. *Pari passu* with the covering of the soil by buildings and pavements malarial diseases disappear. But when this soil is again exposed to the atmosphere evidence is at once obtained that its power to produce malaria has not been lost but was simply in abeyance, because of the absence of an essential factor—oxygen.

This was illustrated in the city of Paris in the years 1811 and 1840, when the soil was extensively moved in digging the canal Saint-Martin, and in the construction of the fortifications. According to Colin this disturbance of the earth was followed by the frequent occurrence of intermittent fevers in the vicinity.

Denudation of a soil covered by forest or rank vegetation is, where other conditions are favorable, a very common cause of increased prevalence of malarial diseases. This is considered by Colin, as it was by Lancisi and other Italian writers, to be the principal cause of the present insalubrity of the Roman Campagna, as compared with its salubrity in former times, when it is said to have been covered by fruit-trees and forests. In India, cutting away the jungle frequently causes malaria to manifest its presence in a most intense form. On the other hand, tropical regions which are covered by a dense forest are remarkably free from malaria. This is true as regards the valley of the Amazon, where, as Galt[2] says: "The medical traveller is more than surprised at the infrequency of malarial fevers on the whole Amazon." This freedom from malarial diseases was ascribed by Bates, the naturalist, to the trade-winds; but, as Galt points out, this explanation can only apply to the lower Amazon, and the dense forest vegetation which covers the face of the country, and even overhangs the margins of the great river, is no doubt a sufficient explanation of this immunity.

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[1] Sir Joseph Fayrer, op. cit., p. 41.

[2] Frank L. Galt: Medical Notes on the Upper Amazon. Am. J. M. Sc., Phila., October, 1872.

These impenetrable forests of Brazil cannot be compared with the terai of India. Here malaria is very intense. But not only are these forest districts so open as to be inhabited by native tribes, but Fayrer says they are swampy, and have a porous soil with a substratum of clay.

Denudation of the soil probably operates to produce malaria, not only by exposing the surface to the direct action of the sun's rays and of the atmosphere, but also by setting free effluvia resulting from organic decomposition, which previously were consumed by the growing vegetation.

M. Colin says: "I think that, far from seeking the cause of fever in the vegetation of marshes, it is rather to be sought in the inverse condition. For me, indeed, the fever is above all caused by the vegetative power of the soil when this power is not brought into action, when it is not exhausted by a quantity of plants sufficient to absorb it. This is so true, that in the swamps themselves vegetation seems to be the condition most efficacious in order to reduce their noxious exhalations" (loc. cit., p. 14).

This was also the opinion of our own illustrious medical author, Dr. George B. Wood, who says: "There is reason to believe that the miasm which produces such deleterious effects upon the animal system is capable of contributing to the nourishment of vegetables. This, perhaps, is one of the reasons why bilious fevers prevail especially in autumn. The vegetation of spring and early summer is vigorous and adequate to the consumption of all the products of the organic decomposition that may be going on in the soil. Among other products the miasmatic exhalations may also be consumed. But toward the close of the season, when many plants have run their course and begun to decline, they cease to appropriate this as well as other food, which is therefore exhaled, if it do not remain in the soil."[1]

INUNDATIONS.—The immediate result of an inundation is beneficial, so far as the production of malaria is concerned, because of the flooding of malarious lowlands and swamps with water. As the amount of moisture in such localities is usually ample for the abundant evolution of malaria, the flood, even when the waters have receded, may leave the face of the country in a better sanitary condition than before. For it is to a certain extent cleansed by the rush of waters. But, on the other hand, the destruction of growing crops, which are left to rot on the surface, the accumulation of masses of vegetable material in certain localities, and the wetting of soils usually dry and non-malarious, cannot fail to increase the evolution of malaria in some places.

Professor Chaillé[2] has given special attention to the study of inundations in Louisiana. In his first contribution to the subject, which related especially to the influence of inundations upon the health of the population of the city of New Orleans, he arrives at the following conclusion: "The evidence, especially in respect to twelve inundations from 1816 to 1861, inclusive, was sufficiently full and satisfactory to justify the general conclusion that the inundations of New Orleans, always partial, had not influenced unfavorably its mortality, whether by yellow fever, by cholera, by malarial fevers, or by diseases generally. On the contrary, the evidence, though imperfect and not fully conclusive, justifies the inference that the deposit and decomposition of filth and any other promoters of disease, which may be due directly to inundations, are more than counterbalanced by the flood, which first covers up the soil, from whence springs so much disease, and then helps to cleanse it." We would remark that, owing to the peculiar topography of New Orleans, it will not be safe to apply the conclusions reached by Dr. Chaillé in this careful research to other cities differently located. The flood which cleanses this city and fills with water the malarious swamps in rear of it, might elsewhere turn into pestilential swamps, land, which under ordinary circumstances was not productive of malaria.

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[1] Practice of Medicine, vol. i., p. 161.

[2] Stanford E. Chaillé, A.M., M.D.: Inundations in Louisiana, their Influence on Health. N. Orl. M. & S. J., June, 1883.

The evidence collected by Chaillé relating to rural districts in Louisiana is not so uniform. As might *à priori* have been expected, the results vary in different localities, being influenced by circumstances relating to the topography of these localities. Still, the evidence collected is in favor of the view that in Louisiana, even in rural districts, overflows are not usually followed by an increase in the amount of sickness from malarial diseases. But, as might be expected, diseases which commonly result from the use of impure drinking-water may appear, as an epidemic, after such an overflow. Thus we read in Dr. Chaillé's valuable paper that:

> Dr. C. M. Smith, of Franklin, President of the local Board of Health, and an ex-President of the Louisiana State Medical Society, reported, July 21, 1882, as follows:
>
> "Since the subsidence of the flood an unusual amount of sickness has prevailed throughout the parish of St. Mary, and especially has this been the case along the Bayou Têche, both in this village and on every plantation. While there has been *less than usual of malarial fever*, dysentery and diarrhœa prevail everywhere in an epidemic form, and in some localities a few cases of typhoid fever have occurred. It is a noticeable fact that the most malignant forms of disease have been observed in the lower portion of the parish, where the lands were submerged on both sides of the river and where no preventive measures were adopted. Seasons of overflow, according to my observations, have heretofore been *invariably followed by healthy summers*, and this accords with the experience of every physician with whom I have conversed. It is evident to me that the widespread prevalence of the diseases named, in a region of country usually healthy, is due to the deposit left by the recent remarkable flood, which, for the first time since 1828, invaded almost every dwelling, and left under many houses stagnant pools containing all the elements of disease."

M. Colin asserts that the overflow of the Tiber does not produce intermittent fevers in Rome. An inundation which he witnessed, in which the waters extended to the Corso, in the centre of the city, was not followed by any notable modifications in the sanitary condition of the population.

We believe that a careful consideration of all the facts relating to inundations will show that where the population of the inundated region depends upon springs and shallow wells for a supply of drinking-water, there inundations will be followed by epidemics of diarrhœa, dysentery, *pernicious* fevers, and enteric fever; but that malarial diseases, properly so called, will not, in most instances, prevail more extensively than usual: this because in regions subject to inundation, the lowlands usually have ample ground-water for the production of malaria, and any addition to this is unfavorable to such production by excluding the ground-air. This of course, does not apply to inundations in an arid, rainless region, having a rich soil, from the overflow of a stream having its origin at a distance. Here the result can scarcely fail to be identical in kind, although not in degree, with that which follows the irrigation of such lands for agricultural purposes.

IRRIGATION.—Fayrer has given us, in his Croonian Lectures, an interesting account of the extent and results of irrigation in India. We learn that, though a great part of the continent of India has an ample rainfall, there are extensive regions where it is insufficient, and where artificial irrigation is resorted to. This is effected by reservoirs, canals, and wells. In all more than six million of acres are now irrigated. Our author says: "The agricultural benefit derived from this system of irrigation is no doubt great, but it has disadvantages, for with the water there is generation of malaria and fever. . . . With the excessive mortality in irrigation districts, the conclusion is inevitable that the true cause is stagnant subsoil water."

In a report of a committee assembled in 1845, under instructions from the Governor-General of India, we read:

> By far the greater part of the evils have not been the necessary and unavoidable results of canal irrigation. In all situations where mischief was prominently marked the natural drainage of the country had been checked or interfered with; stiff and retentive soils saturated with water, and natural disadvantages of site enhanced by excess of moisture. The Eastern Jumna Canal furnishes examples of some of the best and worst results of canal irrigation. In the north and south divisions, where the soil is light, the drainage perfect, and irrigation carried on chiefly by "Rajbuhas," we perceive all the blessings and scarcely any of the evils of the canal. But in the centre division, where the drainage of the country has been greatly obstructed, and the soil is generally more stiff and clayey, the effect on the health of the inhabitants has been the same in kind, and nearly in degree, as in the objectionable portions of the Delhi canals. In the course of our inquiries on the existing canals, we have found salubrity to depend in a great measure on the nature of the soil and the efficiency of the surface drainage.

The results of irrigation in its relation to the development of malaria are well illustrated in Southern California, where a considerable area of land has recently been brought under cultivation by means of irrigation. We are indebted to Dr. J. P. Widney, a member of the California State Board of Health, for an account of the results of this irrigation from a sanitary point of view, and as Dr. Widney's report is very instructive and very much condensed we quote it *in extenso.*

> The lands now under irrigation may be roughly divided into four general classes:
>
> *First.*—Uplands, of which San Gabriel, Pomona, and Riverside may be taken as types. These lands have a firm soil, rather a gravelly clay, which remains moist, but not water-soaked, after irrigation; the slope of the country is regular, and sufficiently rapid to prevent water from standing upon the surface; they lie in what is really the great interior valley of Southern California, corresponding to the Sacramento-San Joaquin Valley of the northern portion of the State, have consequently less force of the ocean winds than the other three classes to be mentioned, have a decidedly higher summer temperature, and are planted chiefly with trees and vines.
>
> *Second.*—River bottoms of sand or alluvium, as those of the Los Angeles and Lower Santa Ana, lying outside of the ranges which shut off in part the wind from Class No. 1. The lands of this second class have the full force of the sea-breeze, broken somewhat by the orchards and rows of trees which line the roads. There is a fair slope, so that water does not remain in pools upon the ground; and under the alluvial surface-soil a substratum of coarse gravel, many feet deep, making under-drainage thorough and complete. Lands planted in trees, vines, corn, and barley.
>
> *Third.*—The sandy bottoms of the San Gabriel River, of much the same character as No. 2, but with a much less rapid surface slope; a wider and more tortuous river-bed, with willow thickets and still water, and the under-stratum of water standing much nearer the surface-soil. The under-drainage in this valley is much less thorough than in the Los Angeles and Lower Santa Ana. Lands planted largely in trees and corn. Sea-breeze the same as in No. 2.
>
> *Fourth.*—Cienaga lands, as in the belt which reaches from the Ballona to the Lower Santa Ana, a length of some forty miles, with a width of from three to five miles. These lands are open plain, near the sea, swept by the full force of the daily sea-breeze; have a heavy soil, of the adobe type; occasional springs and bogs, with natural ponds of water; in winter become very wet; in summer are irrigated extensively by means of

artesian wells, the water from these wells often standing in pools upon the surface and draining off slowly in sluggish ditches, choked by weeds, while the heavy adobe soil gives no under-drainage. These lands are somewhat inclined to be alkaline. Trees are not extensively planted, the land being chiefly in small grain and grass or alfalfa. It is a dairy country.

In tracing the development of malaria through these four classes, it is found that the lands of the first class are almost entirely free from even the slightest trace of its existence.

The lands of the second class show its existence, but not to a sufficient degree to form a marked feature in the endemic causes of disease, except in a few limited areas, which will be again mentioned.

The lands of the third class show the presence of malaria in a notably active form, giving a well-marked type to the summer diseases.

The lands of the fourth class develop, with irrigation, a very active form of malaria, the diseases being largely of a pronounced malarial type, and running often a severe course.

These results do not, at first sight, seem altogether such as we might naturally expect. Class 1, farthest from the sea, with the force of the daily sea-breeze shut off by ranges of intervening hills, planted very extensively with trees, and having a higher summer temperature, develops, with irrigation, practically no malaria; while Class 4, out upon the open plain, only a few miles from the sea, with no intervening hills, planted only to a slight extent with trees, swept daily by the full force of the sea-breeze, and with the lowest summer temperature of all, shows the greatest prevalence of malaria, and in the most virulent form.

There must be a reason for this. What is it?

Upon following the comparison carefully, it will be found that the only feature which bears a constant relationship to the development of malaria is drainage. Class 1, with every other cause at work to produce malaria—greater distance from the ocean, less sea-breeze, higher summer temperature—is thoroughly drained both above and below the surface, and has, practically, no malaria. The only place in this belt where I have, in my own practice, ever found traces of it, is one spot under the lee of a hill, where, by the side of a pond, the drainage is bad and the soil water-soaked.

In Class 2, the only decidedly malarious district I have found, is a region of river bottom extending from the upper edge of Los Angeles City for a few miles on up the river, where the channel widens out and the water runs amid willow thickets, with much wet, boggy meadow land. Farther down the river, as the under-drainage becomes more thorough, the evidences of malaria grow less and disappear, although in the midst of orchards, vineyards, and grain fields, where the land is irrigated many times during the summer. The Santa Ana lands I know less about, but so far as I can learn they follow the same general law.

In Class 3, the same as Class 2, except the wide river bed, the water-soaked, reedy bottoms, and the less thorough under-drainge, malaria begins to show itself actively. These lands resemble more the ill-drained section of the Los Angeles Valley which I have described.

In Class 4, the lands which, by nearly all the known laws governing the development of malaria, except one thing, bad surface and under-drainage, should escape, we find malaria more prevalent and active than in either of the others.

The conclusion seems to be fairly just and legitimate, then, in the absence of any other apparent cause, and from what we know of the close connection between defective drainage and malaria, that in this case the relationship is that of cause and effect. With thorough drainage, the places which, by all other rules, should develop malaria, escape it almost entirely; without drainage, the places which, by all other rules, should be free from it, develop it constantly and actively.

The whole history of irrigation in Southern California goes to impress this lesson: that to escape malaria, drainage must go hand in hand with irrigation; that unless it does, the water which brings wealth also brings disease and death.[1]

DRAINAGE.—We have seen that observers in various parts of the world agree in assigning to stagnant ground-water a prominent place in the production of malaria. That there is no mistake about this is demonstrated by the disappearance, in numerous instances, of malarial diseases as a result of drainage and improved cultivation of the soil; and on the other hand, by the increased prevalence of such diseases in regions where the natural or artificial drainage of the country has been interfered with. The disappearance of intermittent fever from Lincolnshire and other portions of England, as a result of drainage and cultivation, is constantly referred to by English writers of the highest authority. Graves has said: "The extinction of intermittent fever is the most striking, the most eloquent of all the modifications caused by drainage."

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[1] Report of the California State Board of Health, 1880–81.

Parkes refers to the case of Boufaric in Algeria, which was noted for its insalubrity, successive races of soldiers and of colonists having died off. Deep drainage was resorted to and the level of the ground-water was lowered less than two feet. This measure, and a better supply of drinking-water, reduced the mortality to one-third.[1]

Dr. Derby, of Massachusetts, writing in 1872, reports the increasing prevalence of intermittent fevers in localities which for many years had been quite free from these diseases, and attributes this increase to fresh-water obstruction.[2]

Dr. Chamberlain, of the Connecticut State Board of Health, reports that since the completion of a system of drainage in the towns of Fairfield and New Milford malarial diseases, which previously were increasing rapidly, have steadily and rapidly decreased.[3]

M. Colin refers to the beneficial results of drainage and cultivation in various parts of the world, and calls attention to the fact that those who engage in these labors, which in the end are of such sanitary value, often suffer very severely from the effects of malarial poisoning. As an instance he relates the case of Staouëli, in Algeria, where the reclamation by drainage and cultivation of the lands appertaining to a Trappist convent, cost during the first year the lives of 8 monks (out of 28), and of 47 soldiers (out of 150) who were placed at their disposition. Later the greatest change in the salubrity of the place occurred, and in eighteen months there were but 2 deaths out of a population of 152.

CULTIVATION.—In all parts of the world, within the latitudes where malaria manifests its presence, it has been observed that the cultivation of a virgin soil, rich in organic matter, is followed by the endemic prevalence of malarial fevers. This is so well known in the United States that it would be a waste of time to give examples. Other things being equal, the evolution of malaria seems to bear a direct relation to the organic richness of the soil. It is doubtless for this reason that a virgin soil is more prolific in this, as in other respects, and that continued cultivation reduces the producing power. Where the soil is not very rich in organic material the beneficial effects of cultivation, from a sanitary point of view, may be manifest within a few years. But the extreme organic richness of some soils, such as the bottom lands of the Mississippi Valley, for example, is shown not only by their capacity to produce luxuriant crops of Indian corn, cotton, sugar-cane, etc., for a series of years without apparent diminution of productive vigor, but also by the fact that their malaria-producing potency is retained indefinitely. A fertile soil denuded of the luxuriant vegetation with which nature is wont to clothe it, especially in the tropics, gives off malarious exhalations of the most noxious kind. On the other hand, a soil well covered by vegetation of any kind—forest, jungle, or meadow—is less prolific of malaria. A knowledge of this fact has led to attempts to reclaim regions almost uninhabitable because of their insalubrity, by the planting of trees.

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[1] Practical Hygiene, p. 332.

[2] Report of the State Board of Health, Massachusetts, 1872.

[3] American Public Health Association Reports and Papers, 1881, vol. vii., p. 174.

The *Eucalyptus globulus*, an Australian tree, has been especially recommended for this purpose. By some it is thought to be useful not only on account of its vigorous and rapid growth, but because of the aromatic products given off from its leaves, which are supposed in some way to neutralize the malaria given off from the soil. However this may be, the tree is no doubt a valuable one for the purpose indicated, in regions where it can be successfully cultivated; and the reports from Italy and from Algeria, where it has been extensively planted, are favorable as regards the sanitary value of such plantations in malarious regions.

The value of forest trees or of luxuriant vegetation of any kind is easily accounted for, independently of the supposition that they neutralize or consume malaria after its evolution from the soil. In the first place, they require for their growth the same pabulum—organic material in the soil—which seems to be essential for the production of malaria; second, they shade the soil and keep it cool; third, they dry the soil by withdrawing from it a very considerable amount of moisture. According to Parkes, recent observations in Algeria show that the *Eucalyptus globulus* absorbs and evaporates twelve times the rainfall, and extremely malarious places are thus rendered healthy in four or five years (Gimbert).

Petenkofer has calculated that an oak tree having 751,592 leaves, had during the summer months an evaporation equal to 530.1 ctm. (= 212 in.), while the rainfall was only 65 ctm. (= 25.6 in.), so that the evaporation was eight and one-third times the rainfall.[1]

Cunningham[2] states that it has been calculated that two hundred pounds of water are evaporated to grow one pound of woody fibre, either in timber or grass.

VEGETABLE DECOMPOSITION.—What has already been said makes it apparent that the presence of organic matter in the soil is an essential factor in the production of malaria, and, as already remarked, there is no evidence that *pure* sand, or gravel, or clay, under the influence of heat and moisture can produce this morbific agent. But it is also in evidence that a soil containing but little organic matter may produce malaria. It seems probable that but a small portion of the organic matter in a fertile soil comes into action at any one time, for the greater portion of this material remains in the soil, in a latent state, so to speak, and forms a reserve supply sufficient to sustain a luxuriant vegetation for many years. The hypothesis has, therefore, been very generally adopted by recent medical authors that malaria is evolved as a result of the *decomposition* of this organic matter in the soil; for organic matter undergoing decomposition is no longer latent.

Modern researches show that such decomposition is due to the vital activity of living organisms, and that a variety of chemical products are formed while it is taking place, some of which are assimilated by the micro-organisms which are the active agents in the process of decomposition, and some of which are set free.

When we speak of vegetable decomposition as one of the factors concerned in the evolution of malaria, it must be understood that we do not mean that all kinds of vegetable decomposition give rise to the formation of this special poison. The organic matter in the soil is without question mainly of vegetable origin, but it has already undergone a certain kind of decomposition before being incorporated with the soil. Now whether this first decomposition of vegetable matter, which occurs to a great extent upon the surface, can also produce malaria, is a separate question. We know that in certain cases no such result attends vegetable decomposition—in ordinary putrefactive decomposition, for example. Thus the rotten apples and potatoes in a farmer's cellar do not give his family chills and fever; the compost heap is worked over by the farm laborer without fear of evil consequences, etc., etc.

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[1] Practical Hygiene, p. 336.

[2] Dr. J. M. Cunningham: Report to Sanitary Commissioners with the Government of India.

When vegetable material upon the surface of the ground undergoes this primary decomposition it is not easy to determine whether malarious emanations arise from this material or come from the soil. The same difficulty meets us here as in the case of two endemic diseases occupying the same territory. The unusual prevalence of malarial fevers when the vegetation upon the surface is killed by an inundation, or when in the autumn the annual plants and leaves of deciduous trees fall to the ground and decay, may be explained in two ways. We may suppose that malaria is evolved from this decomposing material upon the surface, or that the absence of growing plants favors its evolution in the soil. To study the matter fairly we must exclude one or the other of the confusing elements. Now we have ample evidence that a soil, even if not very rich in organic matter, may produce malaria in the absence of any vegetable material undergoing this primary decay. Such a soil disturbed by the plow, by the digging of canals, or throwing up of railroad embankments, frequently gives rise to intense forms of malarial poisoning. Will vegetable material, by itself, produce the same result?

There are a number of observations indicating that an affirmative answer may be given to this question, but we are inclined to exercise the greatest caution in accepting the evidence heretofore recorded in favor of this view, for the reason that there is so little of it compared with what might be expected if the truth lies in this direction. It is a very common thing, especially among those most accustomed to scientific investigation, to seize upon the first apparent cause which explains a fact in accordance with the investigator's views of etiology, and there to arrest the investigation. The writer has seen an outbreak of cholera, in a previously healthy locality, attributed to a few cabbage leaves, turnip tops, baked beans, etc., scattered about the back yards of dwellings located upon a high and well-drained plateau.

With these remarks, made in the interest of scientific conservatism, we proceed to record the instances at hand in favor of the view that the primary decomposition of vegetable material upon the surface of the ground may give rise to malarial fevers.

Dr. H. F. Norbury, Staff-Surgeon R. N., gives the following case, which occurred in his own person at Cape Colony (Cape of Good Hope), where, he says, malarial diseases are absolutely unknown:

> "This peninsula consists of a chain of rugged mountains acquiring a height of two thousand feet, gradually sloping on the east toward the sea, while on the west a small sandy plain intervenes. The geological formation comprises strata of non-fossiliferous red sandstone, several hundred feet in thickness, based on granite and gneiss, while mounds of gravel are occasionally met with; there is no collection of subsoil water, and the surface is covered with sandy humus thickly studded with bushes; the potable water, moreover, derived from the rain which has percolated the sandstone, is singularly free from organic matter, as I have ascertained by frequent testing.

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> "The present season has been remarkable for its heavy rains, a very few bright hot days intervening. It was on one of these latter occasions, while taking a walk with a friend, that I stood on a heap of moist decaying vegetable matter by the roadside, principally composed of the thick succulent leaves of the Opuntia vulgaris, so as to get a better view of the scenery. The sun was shining brightly on it at the time, when suddenly I inhaled an odor so rank with the peculiar exhalation of decomposing vegetation that I felt nauseated, and was obliged to abandon my position. Exactly four days subsequently, toward noon, I began to feel languid and experienced severe aching pains in the back and limbs, and in the course of an hour I had a violent fit of shivering, with chattering of the teeth, cutis anserina, lividity of the toes and fingers—indeed, all the usual symptoms pertaining to the cold stage of ague. This lasted for an hour and a quarter, during which time I was given hot drinks. Hot-water tins were applied to the surface, etc. ; and then the stage of pyrexia came on, the temperature soon rising to 101.4°, and eventually attaining that of 105.2°. This lasted for an hour and three-quarters, and then began to be succeeded by the sweating stage ; the diaphoresis was profuse, completely saturating the mattress, bed-clothes, etc., and leaving me quite debilitated. Immediately that these symptoms had subsided I took a purgative, combined with a ten-grain dose of quinine, continuing five-grain doses at intervals until some amount of cinchonism was felt. Two days subsequently I underwent a very mild paroxysm, since which I have had no return. I should remark that I had not quitted the district for three months, nor had I been out of the colony for nearly a year, neither have I ever before experienced the slightest symptom of ague."[1]
>
> "Friedel mentions that in the Marine Hospital at Swinemünde, near Stettin, a large day-ward was used for convalescents. As soon as any man had been in this ward for two or three days he got a bad attack of tertian ague. In no other ward did this occur, and the origin of the fever was a mystery until, on close inspection, a large rain-cask full of rotten leaves and brushwood was found ; this had overflowed and formed a stagnant marsh of four to six feet square close to the doors and windows of the room, which on account of the hot weather were kept open at night."[2]
>
> "Dr. Holden relates an instance in which, on board a ship at sea, eight cases of ague occurred from the emanations of a large quantity of mould which had formed in some closed store-rooms which were exposed to bilge-water."[3]
>
> "The rotting of hemp in still water, and the spontaneous decomposition of the indigo plant, in the preparation of that dye-stuff, are asserted to give rise to miasmatic fevers (Wood)."[4]

The cases reported by Tommasi-Crudeli and others, in which attacks of ague have been ascribed to the presence of living plants, in pots, in the sleeping-room of the individual attacked, do not properly come under this head, for in this case we have the same conditions, to a limited extent, as in cultivated soil bearing vegetable products out of doors.

Several observers ascribe attacks of intermittent fever to emanations from decomposing fresh-water algæ, which have been kept at hand in a vessel containing water for purposes of study. My friend, Dr. Harkness, of San Francisco, tells me that it has repeatedly happened to him to be attacked with ague when the algæ in the fresh-water aquaria, kept in his room, died and commenced to undergo decomposition. Hannon says that he suffered an attack of intermittent fever of six weeks' duration while studying the fresh-water algæ during their fructification.[5]

CONDITIONS RELATING TO CLIMATE.

TEMPERATURE.—In a general way the importance of heat as a factor in the production of malaria is shown by the fact that malarial fevers are extremely common and virulent in tropical regions ; that in temperate regions they are less frequent and less fatal ; that they are of rare occurrence during the winter months; and that as we approach the frigid zone they become less frequent, and finally entirely disappear. We shall illustrate this general truth by presenting data relating to the prevalence of malarial fevers in the United States.

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[1] Lancet, Lond., Oct. 5, 1878.

[2] Parkes' Hygiene, 5th ed., p. 343.

[3] Ibid., p. 344.

[4] Practice of Medicine, vol. i., p. 158.

[5] J. de méd., Brux., p. 497, 1866.

The increased mortality from malarial fevers in southern latitudes is shown by the mortality statistics of the last (tenth) census.

"In Grand Group I. (north Atlantic region), the proportion of deaths from malarial fevers to all deaths recorded was 4.56 per thousand, being in the cities 3.02, and in the remainder of the group 5.40 per thousand.

"In Grand Group VII. (the Lake Region) the proportion of deaths from these fevers was 9.74 per thousand, being for the large cities 8.27, and for the remainder of the group 11.88 per thousand.

"In Grand Group IV. (the Gulf Coast) the proportion of deaths from malarial fevers was 65.85 per thousand, being in the city of New Orleans 44.81, and in the remaining portion of the group 77.61 per thousand."[1]

These mortality statistics are valuable in a general way, but for reasons pointed out in the Introduction to this volume, there can be little doubt that a large number of the deaths included in these statistical tables are improperly ascribed to the malarial poison.

The only data obtainable in the United States relating to the number taken sick with these and other diseases are contained in the reports of the Army Medical Department, which relate to the sanitary condition of the troops stationed at the various military posts scattered all over the country.

For our present purpose we shall consider the facts relating to the prevalence of malarial diseases at the posts located upon the Atlantic seaboard; and also at an interior line of posts located upon the banks of the Mississippi and Missouri Rivers. The main facts relating to climate, temperature, and rainfall are shown in the following Tables Nos. 1 and 2. But it must be remembered, in studying these tables, that certain essential facts relating to locality, nature of soil, proximity to marshes, etc., are not represented.

TABLE No. 1.—*Military Stations upon the Atlantic Seaboard.*[2]

STATION.	Latitude.	Total cases of malarial fever in four years.	Total deaths in four years.	Mean strength of command.	Annual ratio per 1,000 of cases to mean strength.	Annual mean temperature.	Annual rainfall.	Mean temperature for months of July, August, and September.	Total rainfall during months of July, August, and September.
							Inches.		Inches.
Fort Preble, Me.........	43°.38'	15	..	47.25	79	45.25°	36.65	64.25°	9.28
Fort Independence, Mass.	42°.20'	16	..	62.25	64	46.46°	40.78	67.19°	10.25
Fort Adams, R. I.......	41°.28'	68	..	271.5	60	47.95°	37.87	66.96°	9.77
Fort Hamilton, N. Y....	40°.37'	716	1	253	697	50.87°	38.18	71.06°	14.81
Fort McHenry, Md......	39°.15'	258	..	201	308	55.08°	33.11	74.16°	10.13
Fort Monroe, Va........	37°.02'	280	1	374	187	58.19°	42.16	77.55°	10.15
Fort Macon, N. C.......	34°.04'	66	..	101.25	162	Not	report	ed.	
Charleston, S C.........	32°.46'	137	..	161.5	212	Not	report	ed.	
Savannah, Ga...........	32°.05'	37	..	58.25	158	66.60°	44.05	80.85°	18.63
Key West, Fla..........	24°.30'	126	1	98.25	317	78.09°	38.58	89.19°	18.34

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[1] Quoted from the Medical News of Nov. 25, 1882.

[2] The data in this and in the following table are obtained from A Report on the Hygiene of the United States Army (Circular No. 8, Surgeon-General's Office, Washington, May 1, 1875). The statistics relate to the period from July 1, 1870, to June 30, 1874, inclusive—four fiscal years.

TABLE No. 2.—*Stations upon the Mississippi and Missouri Rivers.*

STATION.	Latitude.	Total cases of malarial fever, in four years.	Total deaths in four years.	Mean strength of command.	Annual ratio, per 1,000 of cases to mean strength.	Annual mean temperature.	Annual rainfall.	Mean temperature for months of July, August, and September.	Total rainfall during months of July, August, and September.
							Inches.		Inches.
Fort Buford, Dak. Ter..	48°.	66	..	279	59	38.01°	14.01	63.65°	3.40
Fort Benton, Mon. Ter..	47°.45′	12	..	56	53	44.39°	11.42	66.09°	4.34
Fort Stevenson, Dak. Ter.	47°.34′	30	..	116	64	38.46°	13.52	64.61°	5.37
Fort Rice, Dak. Ter.....	46°.40′	82	..	255	80	41.34°	11.98	66.48°	3.08
Fort Ripley, Minn.......	46°.10′	41	..	71	144	35.97°	37.09	61.56°	11.55
Fort Snelling, Minn.....	44°.52′	128	..	117	359	44.93°	20.51	68.10°	7.40
Fort Sully, Dak. Ter....	44° 30′	33	..	231	36	47.01°	16.39	72.05°	5.45
Fort Randall, Dak. Ter..	43°.01′	61	..	198	77	47.56°	15.16	71.86°	3.68
Omaha Barracks, Neb...	41°.20′	284	..	411.75	179	50.80°	31.58	75.71°	9.25
Fort Leavenworth, Kas..	39°.20′	716	..	399.75	449	51.88°	38.88	72.73°	13.73
St. Louis Barracks, Mo..	38°.28′	486	1	302.25	402	No	report.		
Baton Rouge, La.......	30°.26′	1,229	3	171.5	1,803	67.82°	65.87	85.76°	18.36
Jackson Barracks, La....	29°.57′	607	1	257.	590	[1] 66.73°	68.28	80.28°	15.66

These tables illustrate in a general way the influence of heat as a factor in the production of malaria.

In Table No. 1, the rainfall at the various stations is sufficiently uniform to be considered a constant factor, and we have, therefore, only to explain the exceptional instances of salubrity or insalubrity. This we can readily do by referring to the remarks of the medical officers to whom we are indebted for the several reports, and which are recorded in the "Report on Hygiene," from which we have obtained our data. These remarks serve also to illustrate the truth of statements, elsewhere made in the present volume as regards conditions relating to soil, topography, etc.

But a word is required with reference to certain causes of error which cannot be ignored in the consideration of statistics of this kind. First, it must be noted that many of the cases of malarial disease reported are not of local origin. Thus a company may be transferred from a malarious locality in the South to a healthy post in the extreme North; and immediately the sick report at the latter place will show a considerable number of cases of malarial fever, which are due to malarial poisoning which occurred at a distant point. Such transfers of troops, and the arrival of recruits from malarious regions, will account for the greater number of cases reported at extreme northern stations, where the remarks of medical officers stationed at these posts indicate that intermittent fever of local origin is for the most part unknown. Second, it must be borne in mind that a single case may appear in the returns a number of times; for when a man is supposed to be cured he is returned to duty, and his name is taken from the sick report, and every relapse appears in the returns as a new case.

A third source of error, which has already been referred to in the Introduction, is by no means confined to practitioners in civil life. The different signification attached by physicians to the word "malarial," and different views as to etiology, leads to the entry of cases under the heading "remittent fever," which, according to our view, are improperly ascribed to malaria. We suspect that many of the cases of "remittent fever" at northern stations are of this character, for the reason that they bear an unusually large ratio to the cases of intermittent reported, whereas *malarial* remittent fevers are generally believed to result from exposure to malaria in a more concentrated form than that which gives rise to intermittents, or from the combined influence of heat and malaria, and therefore should be in larger proportion in the more southern latitudes. We find, however, that our army statistics show the reverse of this. Thus, if we compare the stations at the head and at the foot of our Table No. 2 we find the difference to be very decided.

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[1] Meteorology for the year 1874 only.

	Latitude.	Cases of remittent, four years.	Cases of intermittent, four years.
Fort Buford, Dak. Ter......	48°	20	46
Jackson Barracks, La........	29°.57′	13	594

One cause of ill-health in northern latitudes, which we believe is not infrequently attributed to "malaria," is that which results from the crowding of individuals in illy-ventilated apartments, and which has very appropriately been called "crowd-poisoning." We strongly suspect that some of the so-called "remittent fever" of northern localities is of this character. The tendency among miners, mountaineers, soldiers and sailors in cold climates is to huddle together in narrow apartments for the purpose of keeping warm, without regard to ventilation, which is necessarily a secondary consideration. A sanitarian who should see the "dug-outs" or stockade houses which many of these hardy adventurers occupy *per force* in northern latitudes during the winter months, would scarcely be at a loss to account for the malaise, and fever of a mild remittent type, from which they often suffer.

The sources of error which we have pointed out diminish, instead of magnifiying, the difference which may properly be ascribed to latitude—temperature—and which is very apparent in our tables. Thus, in Table No. 1, the sum of the ratios for the three most northerly stations is 203, and of the three most southerly stations 687. The difference is still more apparent in Table No. 2, but here the difference in rainfall is so great that a comparison which should ignore this would be unfair, We may compare Fort Buford, Fort Benton, and Fort Stevenson, however, with certain stations in Arizona, where the rainfall is nearly the same. Let us take for example the following:

	Latitude.	Ratio of prevalence of malarial fever.	Annual mean temperature.	Annual rainfall.	Temperature for July, August, and September.	Rainfall for July, August, and September.
				Inches.		Inches.
Camp Lowell..................	32°.12′	694	68.72°	10.16	83.80°	6.45
Camp Grant....................	32°.25′	1,060	66.84°	16.89	83.84°	8.03
Camp Verde....................	34°.57′	978	62.74°	9.71	83.08°	3.76

The sum of the ratios for the northern posts is 176, for the Arizona posts 2,732. Or if it be objected that the summer rainfall is deficient at these stations in Dakota and Montana, we may go down the list in Table No. 2 and take Forts Ripley and Snelling, Minnesota, and Fort Sully, Dakota, which have a rainfall far in excess of the Arizona posts. The figures will now stand:

Southern stations	2,732
Northern stations	539
Excess of rainfall (average for each group) at Northern stations,	12.41 in.
Excess of temperature (average for each group) at Southern stations:	
Annual mean temperature	24.47°
Temperature for July, August, and September	15.28°

Let us now see how we shall account for the exceptional cases in our tables. Referring to Table No. 1, we find the ratio at Fort Hamilton, New York Harbor, to be in excess of that at any station on the Atlantic seaboard south of it. Turning to the report of the Medical Officer stationed at this post we read:

> The features of the country to the north and east of the fort are peculiar. Along the shore the banks are precipitous, and the fort itself stands upon an elevation of about forty-seven feet above low water. Back from the shore the land becomes rolling, and exhibits a series of elevations and depressions till we arrive at Flatlands and Flatbush, names which sufficiently express the character of the surface.
>
> This peculiar feature is the most important element, next to its insular position, in the topography of the fort, the soil being alluvial, consisting for the most part of clay on top, then sand, pebbles, etc., and frequently a second stratum of clay, and the rolling character of the surface producing numerous depressions, some round, some oblong, varying in size from thirty feet in diameter to as many yards. The result is, that the whole country is dotted over with ponds from the surface drainage. . . . It has been calculated that within a radius of a mile about Fort Hamilton there are at least sixty of these ponds. East of the fort, near the new battery, is a marsh of considerable extent, formed by the drainage of the higher land, and imperfectly separated by a bank of sand from tide-water. . . . The natural drainage is bad; the ground being hilly, the water collects in the hollows, forming ponds, that have become filled with rank vegetation, the depth of water constantly varying, being filled during the winter and spring by rain and snow, and in the summer and autumn becoming so nearly dry as to expose almost the entire beds to the direct solar rays.[1]

We can scarcely doubt, after reading this report, that the unusual prevalence of malarial fevers at this station is due to the local conditions described, and especially to stagnant ground-water.

The prevalence of malarial fevers at Fort McHenry, Md., in excess of that shown at stations south of it, is explained by the following quotation from the report of the Post Surgeon:

> The marshy piece of ground spoken of in reference to a portion of the officers' quarters should be filled in, or some means devised to prevent the overflow it is subject to, as it is a fruitful source of disease (op. cit., p. 42).

The unusual exemption from malarial fevers enjoyed by the garrison at Savannah, Ga., is no doubt due to the fact that the troops occupied the upper story of a two-story brick building, situated in the centre of the city. Fort Macon, N. C., which is but little behind Savannah in salubrity, is situated upon a sandy peninsula where it is freely exposed to the pure breezes of the Atlantic.

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[1] Report on Hygiene, op cit., pp. 31 and 33.

The unusual amount of sickness at Baton Rouge, La. (Table No.2), is explained as follows :

> The malarial diseases prevailing at the post are immediately due in great part to the tract of swamp bordering the northern edge of the reservation, and the continuance of winds from that quarter is accompanied by a marked increase in the number and gravity of the cases (op. cit. p. 121).

It is unnecessary to dwell further upon the importance of heat as a factor in the production of malaria ; all authorities are agreed upon this point. According to Dr. Geo. B. Wood malaria is seldom produced at a temperature below 60°.[1] This is also the limit fixed by Drake[2] below which, in his observation, malarial fevers do not prevail.

This corresponds very well with the observations made at our widely scattered army posts. We may take for example Sitka, Alaska, where the rainfall is abundant as shown below :

	Latitude.	Annual mean temperature.	Summer temperature.	Annual rainfall, inches.	Summer rainfall, inches.	Annual ratio per 1,000 of cases of malarial fevers.
Sitka	57°.03′	43.59°	54.84°	65.62	16.54	50

When it is remembered that the garrison at Sitka came from stations within the range of the endemic prevalence of malarial fevers, and was changed at least once during the four years to which our figures relate, it will not be difficult to account for the limited number of cases of malarial fever which appear in the returns, without supposing that they were of local origin.

RAINFALL.—We have already seen that soil-moisture is necessary for the production of malaria ; it is therefore evident that rainfall is an important factor in controlling the prevalence of malarial diseases. In general, arid regions are more salubrious than those in the same latitude having a considerable rainfall. But an excessive rainfall may prevent the development of malaria by flooding the low grounds from which it is usually evolved. The amount necessary to give that degree of soil-moisture most favorable for the production of malaria will depend to a great extent upon the character of the soil and of the subsoil.

A pervious surface-soil with an impervious stratum of clay or rock at some little distance beneath, especially if this presents depressions which hold the water which falls, furnish conditions favorable to the production of malaria with but little rainfall. But if the surface is impervious, the rainfall, instead of soaking into the ground, is to a great extent shed, and carried off in torrents by the surface drainage-channels. For this reason, and because of the exclusion of oxygen from the soil, dry alluvial plains are commonly healthy, while dry sandy plains not infrequently give off most noxious malarial emanations.

The considerable prevalence of malarial fevers at Camp Lowell, and at Camp Verde, Arizona, shows that a rainfall of ten inches is sufficient to promote the evolution of malaria where other conditions are favorable. The ratio of prevalence per thousand of mean strength at these posts is : for Lowell, 694 ; for Verde, 978. In the same territory we find that Camp Mojave has a ratio of only 112, and Fort Yuma of 136. This difference seems to be due to the deficient rainfall at the two last-mentioned posts, for the factor heat is in excess, as shown by the following table:

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[1] Practice of Medicine, vol. i., p. 157.

[2] Diseases of the Mississippi Valley, p. 722.

	Latitude.	Annual mean temperature.	Mean annual rainfall.	Temperature during July, August, and September.	Rainfall during July, August, and September.
			Inches.		Inches.
Camp Mojave....................	35°.06′	73.11°	6.60	91.58°	1.99
Fort Yuma......................	32°.23′	73.75°	2.66	90.92°	1.57

We read in regard to Camp Mojave that:

> The climate is healthy, the winters pleasant, but the summers extremely hot. *There is no rainy season*, though thunder-showers are frequent in July and August. . . . The nights are as hot as the days, the temperature not varying in the slightest degree for hours, so hot that no one can sleep in a house, the whole garrison lying on the open plain, endeavoring to catch the faintest breeze, the walls of the houses becoming so heated as to render the barracks unendurable.[1]

We can easily imagine the result, if, in the same latitude the garrison should remain during the night exposed to the emanations from a porous soil containing stagnant ground-water.

To further illustrate the influence of rainfall, let us compare the sickness from malarial fevers at a post in the dry part of Texas with that at a station in about the same latitude which has an abundant rainfall. For this purpose we select the following:

STATION.	Latitude.	Annual mean temperature.	Annual rainfall.	Mean temperature for July, August, and September.	Rainfall for July, August, and September.	Ratio per 1,000 of cases of malarial fever to mean strength.
			Inches.		Inches.	
Fort Concho, Tex ...	31°.30′	67.95°	11.94	83.65°	2.82	294
Jackson, Miss	32°.18′	66.73°	68.28	80.27°	15.66	1,316

With a summer temperature three degrees higher than that at Jackson we find that Fort Concho has less than one-fourth as many cases of malarial fevers. We read that it is situated at the junction of the North and Main Concho Rivers.

> The surrounding country is a flat, treeless prairie, not susceptible of cultivation, except on the bottom lands where irrigation can be effected (op. cit., p. 195).
>
> The military post of Jackson occupies an elevated spot of about fifteen acres on the west, and adjoining the corporate limits of the city of Jackson. . . . The soil being a light, sandy, porous loam, does not retain water *to stagnate on the surface*, and three *surface-drains* are found sufficient to carry off all surplus moisture (op. cit., p. 134).

The following table, which we copy from Hertz' article on "Malarial Diseases" in "Ziemssen's Cyclopædia," shows in a very marked manner the influence of rainfall as an etiological factor in the same locality during different years. The table which was compiled by Jilek, relates to a noted malarious district of Istria (Pola).

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[1] Report on Hygiene, op. cit., p. 547.

Year.	Rainfall, inches.	Number of persons in every 100 attacked with fever.
1864	18.44	51.4
1863	14.25	48.6
1866	12.10	36.3
1865	8.44	35.4
1867	5.49	22.9
1868	1. 5	14.2

Atmospheric Moisture.—When there is an abundance of moisture in or upon the surface of the soil the atmosphere is humid and mists are of common occurrence. To what extent this atmospheric moisture is necessary or accessory to the production or preservation of malaria it is difficult to say, as soil moisture and atmospheric humidity are so intimately connected in malarious localities that the latter condition cannot well be considered alone. But there are facts which seem to show that an extremely dry air either neutralizes the malarious poison or has no carrying power. On the other hand, a still, moist atmosphere is generally believed to favor the accumulation of malaria, which occurs especially near the ground. It is possible, also, that the poison multiplies in such an atmosphere.

During the daytime the heat of the sun causes ascending currents by which moisture given off from the soil is quickly distributed throughout the lower regions of the atmosphere. If malaria is as abundantly produced, it is at least, for the reason mentioned, not so potent, because not as concentrated in the immediate vicinity of its production, as at night, when the still, moist air retains the malarious exhalations from the soil. That it is not alone the stagnant condition of the atmosphere which makes exposure at night so dangerous in malarious regions is an inference founded upon observations relating to mists and fogs. It is very generally believed in such regions that condensed atmospheric moisture, in the shape of mist or fog, may carry malaria from the low levels, where it is produced, to higher levels, where conditions are not favorable for its local production.

The writer recently had related to him an instance which seems to support this common belief. During the civil war a regiment was stationed upon the summit of Lookout Mountain, near Chattanooga, Tenn., and it was proposed to establish a sanitarium upon this elevated plateau, which seemed to be very favorably located for the purpose. But according to my informant, who was the surgeon of the regiment referred to, the men, who had previously been healthy, soon after removing to this station commenced to suffer from attacks of intermittent fever. No local cause could be discovered to account for this evidence of the presence of malaria, and the surgeon was of the opinion that it was transported by the mists from the valley, which in the early morning arose from the lowlands, ascended the sloping side of the mountain, and like a rising tide flowed over the level plateau upon its summit. My informant states that this mist had a "marshy odor."

The influence of the malaria-laden mists of the Roman Campagna is referred to by Colin as follows:

> Every morning, from the heights of the Quirinal, where our hospitals were located, we perceived at our feet a vast white sheet, which from the gates of the city unrolled

itself as far as the base of the mountains which limit the basin of Rome. Constituted by the nocturnal precipitation of the atmospheric vapors, this fog covered uniformly the entire Roman Campagna. In our immediate vicinity the city itself alone emerged from this sheet of vapor, and in the distance we saw the numerous towns attached to the flanks of the Albian Mountains—Albano, Castel Grondolfo, Marino, Rocca di Papa, etc. To each of these we might have been able, from our observatory, to assign approximately its relative degree of salubrity, according to its elevation above this fog. Thus Albano, at 381 metres elevation above the level of the sea, and Frascati at 336, are only invaded in their lower quarters by this malaria-laden fog, while their more elevated streets belong to the zone of *aria buona* or *fina*. Above these two towns the air is completely salubrious in the little villages of Rocca Priora (717 metres), of Rocca di Papa (807 metres), etc.[1]

OZONE.—The accumulation of malaria at night has been ascribed to the absence of ozone, which is supposed to be produced during the day by the sun's rays (Uhle). It has also been suggested that the abundant presence of ozone may account for the absence of malaria from certain swamps where the conditions would seem to be favorable for its evolution (Hertz). But according to Fox, "There is no evidence to show that ozone destroys the marsh miasm, or is in any way related to malarious disease."[2]

Dr. Fox concludes, however, from his studies of ozone, that it is an agent of great importance in nature, and that it decomposes some of the offensive products of putrefaction. Nevertheless we are compelled to agree with Parkes that "the subject of the presence and effects of ozone, curious and interesting as it is, is very uncertain at present."[3]

WINDS.—The influence of winds upon the prevalence of malarial fevers has been repeatedly observed in many parts of the world, and is one of the strongest arguments in support of the view that malaria is a material substance. For all observations are in accord in showing that it is not the quarter from which the wind blows *per se* which influences the result, but the relative position of certain terrestrial areas which are themselves recognized as sources of the malarial poison. In other words, the influence of malarious winds depends solely upon the capacity of currents of air for transporting the poison from its source to more or less distant localities.

In general, land breezes in malarious regions are charged with malaria, and sea-breezes are not. The insalubrity of these land-breezes depends upon the nature of the surface over which they have passed. If this be dry and sterile they are usually innocuous. But if they come over tropical swamps or jungles, or from rich alluvial bottom-lands saturated with moisture, they may give rise to severe forms of malarial disease in situations where there is no malaria of local origin.

Very great differences of opinion exist among authorities as to the distance over which malaria, in quantity sufficient to produce disease, may be transported by the wind.

According to Tommasi-Crudeli,[4] the malarial poison is ordinarily confined to a height of three or four feet above the surface of a malarious soil. "Above this the air of malarial regions is usually inoffensive, either because the germs are not raised higher by the ascending current of air, or because they are not sufficiently numerous to produce malarial infection." Not only does this author accord but little altitudinal range to malaria, but in his opinion "the theory that malaria may be carried a great distance by the wind is not supported by facts."

Lancisi also accords but a limited capacity for transportation to the winds, and points out the fact that the south wind does not injuriously affect the inhabitants of the city of Rome, although the Pontine marshes lie in this direction, at a distance of forty to fifty kilometres (eighteen to twenty-five miles). Colin, however, points out that it is not the distance which is an obstacle in this case, but the fact that these marshes are not, under ordinary circumstances, the source of the malaria from which the inhabitants of Rome suffer. According to this author, the Pontine marshes are almost innocuous, except when, from an unusually hot or dry season, the level of the water in them is lowered and the subjacent mud is exposed to the action of the atmosphere. In this case the inhabitants of the adjacent villages suffer cruelly, as in the year 1865 ; but it is the Roman Campagna which is responsible for the malarial fevers for which this part of the world is so celebrated. In the city of Rome the low-lying places along the Tiber are said by Colin to be less subject to malarial fevers than higher points—the ancient Roman hills, which, on account of their elevation, receive from the slightest atmospheric currents the malarial emanations from the plains, while they serve to protect from these winds the other quarters of the city.[1]

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[1] Op. cit., p. 48.

[2] Dr. C. Fox: Ozone and Antozone, 1873, p. 147.

[3] Op. cit., p. 443.

[4] J. d'Hyg., Par., Sept., 1880, p. 459.

M. Guérard, a French author of repute, supposes that the unusual prevalence of fevers in Europe at certain periods—epidemic prevalence—is due to the transportation of germs by atmospheric currents from the continent of America, and especially from the Gulf of Mexico (Colin). Surgeon Charles Smart, of the United States Army, has also suggested the transportation of germs from a distant malarious locality, and their subsequent deposition by the falling rain or snow in high altitudes, as a cause of the so-called "mountain fever," which he thinks it probable may result from drinking such "malarious waters."[2]

This belief in the transportation by the wind of the malarial poison, in an efficient form, to a great distance from its source, and especially over intervening bodies of water, has not met with much favor among medical authorities, and is opposed by numerous observations.

Dr. Wood says: "Winds appear to be capable of carrying miasmata, either enveloped in clouds and fogs or otherwise, a very considerable distance ; according to MacCulloch, even so far as five or six miles."[3]

Hertz says: "We may admit the agency of the wind as a carrier of miasm for a short distance ; but when it comes to stretches of many miles it is no longer to be taken in account."[4]

Lancisi relates the following: "Thirty ladies and gentlemen had sailed to the mouth of the Tiber on an excursion of pleasure. Suddenly the breeze shifted to the south and began to blow over a marshy tract of land situated to windward of them. Twenty-nine of the thirty were immediately after attacked with tertian ague" (Watson).[5]

Dr. Watson, referring to the fact that in malarious regions the crews of ships which are anchored a few thousand yards from shore do not suffer from the fevers which are often extremely prevalent and fatal among those who remain permanently or temporarily on shore, says: "It is probable that this peculiarity has led to an erroneous and contracted estimate of the space through which the poisonous effluvia can be carried upon land by the wind. Although the distance to which they are capable of being so conveyed without losing their morbific power has never been precisely defined, there can be no doubt that it is considerable. In Italy, according to Dr. MacCulloch, the poisonous exhalations of the lake Agnano have been ascertained to reach as far as the Convent of Camaldolio, situated on a high hill three miles distant."[1]

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[1] Op. cit., p. 50.

[2] Am. J. M. Sc., Phila, Jan., 1878.

[3] Practice of Medicine, vol. i., p. 160.

[4] Ziemssen, vol. ii., p. 572.

[5] Practice of Physic, Am. ed., 1845, p 463.

Sir Gilbert Blaine, in speaking of bilious remittent fever, says: "I have known a hundred yards in a road make a difference in the health of a ship at anchor, by her being under the lee of marshes in one situation and not in another. It is difficult to ascertain how far the influence of vapors from woods and marshes extends; but there is reason to think that it is to a very small distance. When the ships watered at Rock Fort they found that if they anchored close to the shore, so as to smell the land-air, the health of the men was affected; but upon removing two cables' length no inconvenience was perceived."[2]

A marked difference in the amount of sickness resulting from exposure to breezes from a malarious swamp noted in dwellings but a short distance apart may be due to the direction in which these face rather than to the difference in distance from the source of the malarial poison. Other circumstances also, such as the proximity of water, or the shelter furnished by an outer row of dwellings, by trees, etc., must be considered, for it is scarcely probable that the sharply drawn line observed in such cases as the following can be due to distance alone. M. Rigaud de l'Isle says:

> About the end of 1810 I was at Civita Vecchia, in Italy. Passing through St. John's Place, which is a pretty regular square, I was shown one whole side where the inhabitants had been much afflicted with diseases occasioned by bad air, while those on the opposite side had almost escaped. What could be the cause of such an extraordinary difference between houses so near to one another? Dr. Nucy, an intelligent physician, pointed out to us that the former faced south, so as to receive directly the southeast winds, which arrive saturated with miasmata from marshes on the coast.[3]

The following is related by Dr. S. Meredith:

> At the Loajan tea factory the laborers' cottages were erected in two rows facing each other, on a piece of ground about fifty yards wide and several hundred in length, and situated on the left bank of the Shansi River. The back of one row of houses was toward the river, a few yards of space intervening, covered with shrubs, but no grass. The other row was toward the grassy ground; the jungle came quite up to the houses. All the houses were built of plaited bamboo and thatch. The laborers were therefore of the same kind, living on the same food, and exposed to the same atmospheric conditions; the only difference was that one row was close to the jungle and the other at some little distance. The men in the row close to the jungle suffered much more from malarious diseases than those in the row of houses nearer the river.[4]

Although, as we have seen, the wind may bring malaria from a distance to healthy locations, it is on the whole a sanitary agent of the greatest importance, as it promptly dilutes and dissipates the malarial emanations of the soil over which it sweeps.

Many regions which would doubtless be pestilential but for the purifying influence of the prevailing winds are quite salubrious, although the local conditions may be favorable for the production of malaria. For this reason the sea-coast and small islands are commonly more salubrious than the interior. This is especially true of low islands which come within the influence of the trade-winds. Thus we read that at the Fiji Islands, although the climate is strictly tropical, "the trade-winds modify the temperature and prevent the accumulation of miasmata from the enormous masses of decaying vegetable matter, so that malarial diseases are rare."[1]

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[1] Practice of Physic, Am. ed., 1845, p. 463.

[2] Diseases of Seamen, p. 221 (quoted from Bartlett).

[3] Johnson on Tropical Climates, p. 123.

[4] Report English Army Med. Dep , 1870, Appendix, p. 239.

The absence of malarial diseases from the Bermudas has been noted by several writers. The Sandwich Islands also are comparatively free from these diseases, as are the Society Islands, and in general the smaller islands of the Pacific and Gulf of Mexico.

TOPOGRAPHICAL CONDITIONS.

MOUNTAINS.—The sloping sides and elevated peaks of mountains are commonly free from malarial diseases, but these are often very prevalent at the base, especially of wooded hills and mountains, as the drainage from the slopes is here checked and the soil is often saturated with water and may even be boggy for this reason. Mountain valleys, when the temperature is sufficiently elevated and the soil contains stagnant ground-water, are often prolific sources of malaria. Elevation, except in so far as it favors drainage, and is attended with a reduction in the temperature belonging to places at the sea-level in the same latitude, seems to be a matter of no importance.

According to Parkes, malarial fevers have been known to prevail during the rains at Kussowli (6,400 feet), at Subathoo (4,000 feet), and at other Himalayan stations.[2]

Hertz states that on the Tuscan Apennines fevers are to be found at the height of 1,100 feet; on the Pyrenees at 5,000 feet; on the island of Ceylon at 6,500 feet; and in Peru at 10,000 and even 11,000 feet.[3]

VALLEYS.—Other things being equal, narrow valleys are less salubrious than open plains, and the more they are protected by the surrounding hills from the purifying action of the prevailing winds, the more unhealthy they are apt to be. On the other hand, when a narrow valley is swept by the winds, it may serve as a channel through which malarial emanations are carried high up the mountain's side. "It has drifted up even to the summits of the Neilgherries, 7,000 or 8,000 feet."[4]

ISLANDS.—In speaking of the purifying action of sea-breezes we have already had occasion to refer to the exceptional salubrity of small islands.

Finally we may conclude this section by saying that, in general, those topographical conditions which favor the accumulation of stagnant ground-water, and which interfere with the purifying influence of atmospheric currents, are favorable to the development, and concentration near the surface of the ground, of the malarial poison; while those conditions which favor natural drainage and free access of the wind to malarious localities influence in a favorable way the salubrity of a place.

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[1] Staff-Surgeon Messer, in Med. Times & Gaz., Lond., January 9, 1875, p. 35.

[2] Op. cit., p. 667.

[3] Ziemssen, vol. ii., p. 566.

[4] Indian Sanitary Report, Mr. Elliot's evidence, vol. i., p. 250.

CHAPTER III.

SPECULATIONS AND RESEARCHES RELATING TO THE NATURE OF MALARIA.

THE highest medical authorities in all parts of the world, while recognizing the fact that there is such a thing as malaria, generally concur in the statement that we know nothing definite as to its chemical and physical characters. This is the verdict of the older authors, Wood, Bartlett, Watson, Aitken, and MacCulloch, and also of more recent authorities—Hertz, Colin, Fayrer, and others.

The present writer regrets that he does not find himself in a position to give a more definite answer to the question, What is malaria?

Having made this confession, it may be thought that in a practical work upon "Malaria and Malarial Diseases" the example of the illustrious men named might well be followed, and speculations relating to the nature of this unknown agent avoided. But this is the age of experimental researches, and it is generally recognized that we must depend upon the experimental method for the solution of this problem. It therefore becomes necessary to record the efforts which have been made to this end; for the direction of these researches in the future, as in the past, must necessarily be controlled by speculations relating to the nature of the poison, and it is important that these speculations should be well considered and founded upon observed facts, if they are to bear fruit hereafter. We believe, therefore, that a systematic statement of the researches thus far made, and of the speculations which have led to them, will be of value as indicating the direction which future investigations should take.

The Italian author Lancisi[1] (1695) was the first to demonstrate in a definite manner the fact that malarial fevers are caused by a material substance—malaria—and to point out the conditions which control its production. His view seems to have been that the poison is of a gaseous or aëriform nature, and this has been the commonly accepted belief until within the past few years. Recently, however, there has been a growing disposition to believe that the malarial poison is particulate and organized; in other words, that it is a living "germ" or micro-organism. This is not a new view, as it was formulated by Lucretius (95 B.C.) and has been suggested by Linnæus (1778) and others. In our own country prominence was given to this theory of causation by the able paper of Dr. Mitchell, of Philadelphia, published in 1859.

Various suggestions have been made as to the exact chemical nature of malarial emanations by those who suppose them to be of a gaseous form, but the chemists have thus far failed to demonstrate any special ingredient in marsh-air or in marsh-water to which specific poisonous properties, of the kind which the hypothetical substance malaria possesses, can be properly ascribed. As examples of the explanations based upon this view of the nature of malaria which have been offered, we may mention the suggestion of Dr. Hempstead,[1] that hydrocyanic acid is probably the cause of autumnal fevers; that of Professor Daniel (1841), who inferred, from his having detected sulphuretted hydrogen in the water of certain African rivers, that this gas might be the noxious ingredient of the air of marshes (Wood); and that of Wilson,[2] who supposes that ammonia united with a ferment is the agent in question.

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[1] De noxiis paludum effluviis.

Our knowledge of the chemistry of marsh-air is summarized by Parkes as follows:

> The air of typical marshes contains usually an excess of carbonic acid, which amounts, perhaps, to .6 or .8 or more per 1,000 volumes. Watery vapor is usually in large quantity. Sulphuretted hydrogen is present if the water of the marsh contains sulphates, which in presence of organic matter are converted into sulphurets, from which SH_2 is derived by the action of vegetable acids. Carburetted hydrogen is also often present, and occasionally free hydrogen and ammonia, and, it is said, phosphoretted hydrogen.
>
> Organic matter also exists in considerable quantity. Discovered by Vauquelin (1810 to 1811, in the air collected over the Languedoc marshes), by De Lisle, and again by Moscati (1818, in the air of a Lombardy rice-field), and examined more recently by Boussingault (1829, 1839), Gijot (1859), and Becchi (1861), the organic matter seems to have much the same character always. It blackens sulphuric acid when the air is drawn through it; gives a reddish color to nitrate of silver; has a flocculent appearance and sometimes a peculiar marshy smell, and heated with soda-lime affords evidence of ammonia. The amount in Becchi's experiments was .00027 grm. in a cubic metre of air (=.000118 gr. in one cubic foot).[3]

It is hardly worth while to combat the idea that malarial fevers are produced by any of the above-mentioned gases, which are well known to chemists, and the toxic properties of which are quite different from those exhibited by the unknown agent malaria.

But as regards the organic matter present in the air of marshes and other malarial localities, we cannot speak with the same confidence. The very tests by which this is known to us change its chemical structure, and it is impossible to say what its physiological effects might be if administered unchanged to healthy men and animals. We do know, however, that certain complex nitrogenous substances produce most violent toxic effects in very minute doses. As examples of this we may mention the septic poison—*sepsin*—which has been obtained by Bergmann, by Panum, and by Burdon-Sanderson from putrid animal matters; the ptomaines, which resemble the vegetable alkaloids in their reactions, and which have been studied by Selmi and by Gautier, who obtained them not only from putrid blood but also from the normal secretions of healthy persons; and the proteids obtained by Weir Mitchell and Reichert from serpent venom. We may remark that the septic poison produces fever of an intermittent character, and that in several respects its action resembles that of the malarial poison. This is seen in various surgical injuries where fever results from the absorption of the products of decomposition from a concealed pus-cavity, from the surface of an open wound not treated antiseptically, etc.

It has been suggested that malaria may be a poison of this kind, and there is nothing in the circumstances which govern its production to contradict this view. We can easily understand how such a poison might be formed in the soil as a result of the vital activity of certain micro-organisms, the pabulum for the rapid multiplication of which would be found in the organic matter which appears to be an essential element for the production of malaria. But the poisons of this kind of which we have any knowledge are not volatile, and it is not so easy to account for the presence of such a poison in the atmosphere. However, this may perhaps be explained without great difficulty, and the main question is whether the phenomena of malarial poisoning can be accounted for upon the hypothesis that malaria is a poison of this kind.

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[1] West. J. of M. & Phys. Sci., Cincin., 1828-29.

[2] Thomas Wilson, Esq.: An Inquiry into the Origin and Intimate Nature of Malaria, Lond., 1858.

[3] Practical Hygiene, p. 112.

In a paper contributed to the London *Lancet* (liii., No. 2) Dr. H. Bence-Jones offers a theory of the *modus operandi* of infection and of pathogenic action upon the supposition that malaria is a poison of the kind indicated. He says:

> Ague ferment is probably a highly complex nitrogenous substance, capable of being dried and carried by the wind far from the place where it was produced. It enters by the mouth with the dust, and, like animal or vegetable alkaloids, it passes from the blood into every texture of the body, and acts on each much or little, according to its chemical properties. Probably it acts most strongly on the nerves that regulate oxidation, causing for a time contraction of the arterial vessels and consequent suboxidation everywhere. The increased obstruction of the small arteries reacts on the tension of the blood, and this produces increased contraction of the heart, which continues to increase until the obstruction yields. and a state of peroxidation is set up, by which the poison is partially destroyed. During the remission, probably the poison is reproduced until sufficient is formed, in from one to three days, to go through the same action again.
>
> This theory of ague admits of a reasonable explanation of the action of quinine and arsenic in stopping the paroxysms of the complaint. On the ague poison itself quinine and arsenic may have no action, but they pass into every texture from the blood, and, combining with the nervous substance on which the ague poison acts, they form a compound on which the ague poison is incapable of producing an effect before it is oxidized and destroyed.
>
> The ague poison, unlike the small-pox or typhus fever ferment, instead of protecting the body by making it incapable of undergoing the same action again, makes the nerves more ready, on the slightest renewal of the poison, to undergo the same action again; so that it has been said that the ague poison may lie dormant for years. It is far more probable that a much smaller quantity of the poison can produce the return of the symptoms than that the original ferment should retain its properties for months, or even for years, after its first action had passed by. In this respect, and in some others, the action of ague poison proves that it is a very peculiar ferment, and hence, though I have placed it near to the typhoid ferment because of its origin, I must shortly point out to you the different effect which the true typhoid ferment produces.

The weak point in this explanation is the supposition that "during the remission probably the poison is reproduced until sufficient is formed, in from one to three days, to go through the same action again." It is difficult to believe that a non-living ferment, formed in the first instance in the soil, should be reproduced in the body of a living animal, except as a result of the vital activity of the micro-organisms which produce it external to the body. And the cases of relapse at a remote period after exposure, are especially hard to reconcile with this explanation. We must suppose that a certain amount of this ferment is stored away in the system, and that weeks and months after a cure has apparently been effected by the administration of quinine, the poison again multiplies sufficiently to produce a paroxysm of intermittent. The reproduction of the poison according to this hypothesis must be effected by some of the normal histological elements of the body—*e.g.*, gland cells, epithelium cells, nerve cells; for to suppose that the poison multiplies itself, is to place it at once in the category of living ferments; for living organisms alone are capable of self-multiplication.

The writer is not, however, inclined to dismiss this hypothesis as to the nature of the poison as untenable, and objects only to the supposition that the paroxysms of fever are due to its reproduction in the body independently of the micro-organisms which we must suppose to be concerned in its production in the soil of malarious regions.

Two other explanations are open to us upon the hypothesis that the malarial poison is a complex nitrogenous compound produced in the soil in the way indicated.

First.—Malarial poisoning may be an intoxication in which the toxic agent is not reproduced within the body, and in which the paroxysmal febrile attacks are secondary phenomena, resulting remotely from injury to the nervous system caused by the direct action of the poison, and immediately from a secondary cause, such as chill, indigestion, vitiated secretions, etc. This possibility will receive further attention in the article devoted to "Malarial Poisoning."

Second.—The poison may be reproduced within the body by the same micro-organisms which are concerned in its production in the soil, and which may gain entrance to the body by the respiration of an atmosphere in which they are suspended, or by the ingestion of malarious waters.

Another hypothesis is that malarial poisoning results from infection by low organisms, present in a malarious atmosphere, which *directly* produce the phenomena ascribed to malaria, but which do not multiply within the body of the infected individual.

Finally, the malarial poison is thought by many to be *a living germ, capable of self-multiplication within the body* of an infected individual, as well as in the malarious soils which are its normal habitat.

According to this view the morbid phenomena are accounted for by the direct action of the malarial parasite, and the periodicity which characterizes malarial fevers is supposed to result from circumstances relating to the life-cycle and periodic development of this micro-organism.

The observations and experimental researches bearing upon the two last-mentioned hypotheses must be considered before we can attempt to estimate their value.

In this country Dr. Salisbury,[1] of Cleveland, Ohio, was one of the first to attempt to solve the malaria problem by direct observation and by experiment. His microscopical researches led him to the conclusion that a unicellular alga, belonging to the genus *Palmella*, was the malarial germ. The evidence offered in favor of this view consisted in the finding on the surface, in marshy localities, great quantities of this little plant; in the presence in the atmosphere of spores of the same; and in the detection in the sputa of persons suffering from intermittent fever of cells believed to be identical with these. Also the alleged production of typical attacks of intermittent, in four individuals, as the result of exposure in a bed-chamber in the open window of which fresh clods from the marshy soil containing this *Palmella* were placed. The attacks are said to have followed such exposure at intervals of ten, twelve, and fourteen days, and to have been cured by quinine.

The evidence offered in Dr. Salisbury's paper, even if we exclude the possibility of errors of observation, is entirely inadequate to sustain his conclusion that this *Palmella* bears a causal relation to intermittent fever. And, as these observations have not been confirmed by subsequent investigations we can accord them but little value. We may remark, however, that the experiment reported is one which, it seems to us, is more likely to lead to definite results, if repeated with sufficient care and supplemented by careful microscopical researches, than certain later experiments, in which culture-fluids, inoculated with micro-organisms from swamps, have been injected subcutaneously into animals not demonstrated to be susceptible to malarial poisoning.

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[1] Am. J. M. Sci., Phila., January, 1866.

In 1870 M. Bolestra reported the results of his microscopical investigations made in the vicinity of Rome.[1] An examination of the water of the Pontine marshes and of those of Ostia and of Meccarebe showed that they were filled with infusoria of different species, varying with the condition of the water and the degree of its corruption. Among these various organisms one in particular attracted attention. This is said to be a little plant, most abundant in water of marshes which is in a putrid condition, and which resembles slightly the *Cactus Peruvianus.* This alga rests upon the surface of the water; it is mixed with a quantity of greenish-yellow, transparent spores, $\frac{1}{1000}$ mm. in diameter; there are also sporangia of $\frac{1}{100}$ to $\frac{1}{300}$ mm. in diameter, in which these spores are included. This alga is said to grow rapidly in the presence of oxygen and under the influence of the direct solar rays, and especially in the presence of decaying vegetation. The above-described spores were also found in the air of Rome and its environs, and they were still more abundant in condensed atmospheric moisture obtained from the vicinity of marshes. The numerous observations of Bolestra led him to the conclusion that these spores, or some toxic principle connected with them, constitute the cause of paludal fevers. No evidence other than the finding of the plant and spores in question, is, however, adduced in favor of this belief, and the observations recorded are introduced here, not because they are supposed to have any particular scientific value, but as a part of the history of the researches which have been made with a view to discover the malarial "germ."

We may next refer to the investigations of Dr. Lanzi, of Rome, made in 1876. The microscopic fauna and flora of the Pontine marshes and of the marshes of the Roman Campagna also occupied the attention of Dr. Lanzi, who reports the discovery of a peculiar alteration which the algæ in these situations are subjected to. The cells become filled with dark granules, which become more abundant as the algæ die and pass into a state of putrefaction. The chlorophyl disappears as these granules increase in number, and finally the cells become quite black from the accumulation of these dark-colored bodies, which Lanzi believes to possess the properties of a ferment, and to be identical with *Bacteridium brunneum* of Schroeter. They are found in abundance in the dust of the Campagna, and can be cultivated by using this to inoculate a culture-medium. According to Lanzi, the pigment-granules found in the spleen and liver of persons suffering from malarial poisoning are identical with these dark granules found in decaying algæ. We pass this alleged discovery without remark, except that it still lacks confirmation.

Next in point of time we find recorded the discovery of Eklund, of Sweden.[2] This author collected mud from malarious marshes, and heaps of sea-weed from the beach in malarial localities, and placed this material in saucers which were covered with glass vases. These were exposed to the direct rays of the sun upon a balcony. The condensed moisture upon the inside of the glass vases was examined by the microscope and the malarial parasite found. It is named *Limnophysalis hyalina*. According to Eklund, this parasite had previously been observed by Lemaire and Gratiolet (1867) and by Cauvet (1876). It is a fungus which develops directly from a mycelium, which is simple or dichotomous, hyaline, and extremely slender. In presence of heat, moisture, and decomposing vegetable material the mycelium grows in length and sporangia or conidia are formed. These are transparent at first, but when the sporangia are entirely ripe the spores have a brown color. The *Limnophysalis* is found in the blood of those attacked with intermittent fever. To demonstrate its presence Eklund draws blood by puncture with a needle from the superficial capillaries in the region of the spleen. This is received in capillary tubes which are hermetically sealed. Before being examined the blood is diluted with solution of nitrate of potash. In every case the blood of patients with intermittent fever was found to contain the *Limnophysalis hyalina*. It was also found in the urine, where its presence indicates that the patient is liable to a relapse.

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[1] Report to the French Acad. of Sciences, Arch. gén. de méd., Par., September, 1870.

[2] Arch. de méd nav., Par., 1878, xxx. p. 6–11.

We come now to the discovery of Klebs and Tommasi-Crudeli,[1] announced in 1879. This is entitled to more consideration than those previously mentioned, because of the painstaking nature of the investigation, and careful record of observations which form the basis of the alleged discovery; and because considerable independent evidence has since been presented in favor of the view that the *Bacillus malariæ* is the much-sought malarial germ.

The morphological characters of this bacillus are described as follows: In the earth of malarious districts are found numerous, shining, oval, and mobile spores, .95 of a micro-millimetre in diameter. In culture-fluids these spores develop into long threads, which are at first homogeneous, but later divide into segments. It is mentioned as a peculiarity of this bacillus that the spores are at the two extremities of the segments, and in some cases a third spore is seen in the middle of a rod.

The evidence offered in the original memoir of Klebs and Tommasi-Crudeli, in favor of the belief that this bacillus is the cause of malarial fevers in man, is derived from experiments made upon rabbits, in which culture-fluids containing the bacillus in question, and washings from malarious soils, were injected subcutaneously. The results of these experiments are summarized as follows in the London *Medical Record:*

> 1. The poison is contained in great quantities in malarial districts at seasons when no fever is prevalent.
> 2. At such seasons it can be collected from the *air* immediately above the soil by an aspirator.
> 3. Stagnant water does not usually appear to contain organisms peculiar to malaria.
>
> (*a*) Rabbits inoculated with washings of soil, or with fluids in which the bacillus had been cultivated, suffered from intermittent fever, the interval being in some cases 80 hours.
>
> (*b*) *Filtered* liquids caused only slight symptoms, even if five times the original quantity was used.
>
> (*c*) All the animals with intermittent fever had marked splenic enlargement, nine or ten times the normal size.
>
> (*d*) Many of the spleens contained black pigment, especially those from graver cases, just like the spleens of persons suffering from ague.
>
> (*e*) The bacilli were found in the spleen and marrow of animals, as well as in the

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[1] Sulla natura della Malaria. Trans. R. Acad. Lincei, iii., 1879.

soil. They were at first ovoid, mobile, shining spores, which developed in the body, as well as in cultivation apparatuses, into long threads, homogeneous at first, but soon dividing into sections, each of which gives rise to a new thread.

(*f*) These bacilli could not develop without oxygen, and required a richly-nitrogenized medium for their growth and cultivation.[1]

The importance of this alleged discovery induced the National Board of Health, soon after the publication of the first report published by Klebs and Tommasi-Crudeli, to undertake control experiments in a recognized malarial locality in this country. The writer, who had established a laboratory in New Orleans for the purpose of studying the micro-organisms present in the atmosphere of that city, was therefore instructed to repeat the experiments of Klebs and Tommasi-Crudeli, and during the autumn of 1880 devoted a considerable portion of his time to this investigation. The results obtained were not favorable to the view that the fever produced in rabbits by the injection beneath their skin of infusions of swamp-mud, etc., was a truly malarial fever; and, for reasons stated below, the conclusion was reached that the evidence offered by Klebs and Tommasi-Crudeli in their first report, which alone had been published at this time, was unsatisfactory. The full report of these investigations is given in Supplement No. 14, *National Board of Health Bulletin*, published in Washington, D. C., July 23, 1881. A few extracts from this report are given below:

It seems to me that nothing short of a paroxysmal fever, exhibiting marked periodicity as to the recurrence of the paroxysms, and a sufficient number of them to remove the suspicion of apparent periodicity from accidental causes, can be accepted as proof in an experimental investigation of this nature.

I do not find such proof in the temperature charts of Klebs and Tommasi-Crudeli, nor do I find it in my own charts; and my observations give me little confidence in changes in the dimensions of the spleen, the presence of black pigment, and an increase in body-weight, as evidence of malarial infection in an animal which, so far as we know, is not susceptible to the influence of the malarial poison when exposed to it in the usual manner in which it manifests itself among the human inhabitants of a malarial region.

In order, however, to do these authors justice, I shall quote from their memoir sufficiently to enable the reader to judge for himself of the nature of the evidence upon which they rely. . . .

"Attention is called to the fact that in the 'Roman fever' it often happens that an intermittent paroxysmal fever is converted into a continued or sub-continued form and entirely loses its characteristic type."[2]

REMARK.—A continued fever is produced in the rabbit by the subcutaneous injection of a variety of substances, and this fever sometimes has a remittent character when there is no suspicion of malarial infection.

The writer has already, in the Introduction to the present volume, given reasons for the belief that the continued and sub-continued fevers known as "Roman fever" are not strictly malarial, and that, while they are undoubtedly often complicated by malarial poisoning, they owe their continued form to another etiological factor. This belief is strengthened by the experiments of Klebs and Tommasi-Crudeli on rabbits and by subsequent experiments by the last-named savant.

"In a recent report (March 18, 1883) to the Italian Minister of Agriculture, Tommasi-Crudeli refers to the production of intermittent (?) fevers in the lower animals by the subcutaneous injection of the blood of malarial-fever patients, and states that he made extensive preparations to continue his experiments in this direction during the year 1882 ; but he was unable to carry out his intention for the reason that not a single case of *pernicious* fever was received during that period into the Roman hospitals.'[1]

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[1] Quoted from Fayrer, op. cit., p. 27.

[2] Quotations from original report of Klebs and Tommasi-Crudeli, as published in Trans. R. Acad. Lincei, iii., 216-220, 1879.

"Here, then, we have a confession which makes it evident that the *pernicious fever* ascribed to malaria by the author referred to differs from ordinary malarial fevers—intermittents and remittents—which also prevail in Italy, in the essential particular that it is an infectious disease and may be transmitted to the lower animals, as well as in the fact that it is a continued rather than a paroxysmal fever.

"The writer has long suspected that the continued pernicious fevers of the Roman Campagna, and of other parts of Italy, differ essentially from the ordinary intermittents and remittents of this country, and that, while there is undoubtedly a malarial element, in a certain proportion of the cases at least, there is another etiological factor to which the continued and pernicious form of development manifested by the morbid phenomena must be ascribed. We know that malaria may be associated with the specific poison of typhoid or of yellow fever in such a way as to produce atypical forms of these diseases, and it seems not improbable that the Roman fever is in truth one of these mixed or hybrid forms of disease. In this case the bacillus of Klebs and Tommasi-Crudeli, if it has any etiological import, is probably the factor to which the continued and pernicious form of this fever must be ascribed, rather than the malarial germ which the authors named had undertaken to discover."[2]

Returning to the writer's "Special Report to the National Board of Health," we find the following extract from the memoir of Klebs and Tommasi-Crudeli.

"The diminution in the weight of the body, which is generally observed in other fevers, is not found in malarial fevers, it is only noted at a later stage of the disease. In the first days of the fever, especially when it is of a true intermittent type, the appetite increases, and this explains why there is no decrease in weight. This peculiarity is a characteristic sign of the malarial infection which must be taken into consideration during researches on animals."

REMARKS.—I am not aware that the truth of this statement is generally admitted by the profession, and even if we accepted it as demonstrated so far as man is concerned, very carefully conducted experiments would be required to eliminate the possibility of gain in weight from natural growth, or from improved conditions as to food and comfort.

In my Experiment No. 6, in which a rabbit was injected with putrid urine, and suffered an attack of fever which produced death in twelve days, a gain in weight of 103 grms. occurred. This was a young rabbit which was growing rapidly at the time the experiment was made. I have observed a marked increase in size in other rabbits experimented upon in which the fact was not verified by weighing.

"During a septic process the form of the spleen is modified in such a way as to present a rounded aspect, or a rotundity of its edges, while in the malarial infection the splenic tumefaction appears like a regular uniform swelling of the whole organ, and the transverse sections resemble those of a normal spleen, but larger in every direction."

REMARKS.—I have not been able to discover any marked differences in form between the spleens of rabbits which have succumbed to unquestionable septicæmia, and those in which an attempt was made to produce malarial infection by the subcutaneous injection of material obtained by the methods of Klebs and Tommasi-Crudeli from malarial localities near the city of New Orleans. As to the size of the spleen, which I have compared directly, by weight, with the weight of the body (see Experiments 4, 6, 7, 9, 13, 14, 16, 28, and 33), instead of adopting the plan of Klebs and Tommasi-Crudeli, which consists in measuring the length, breadth, and thickness, for the purpose of comparison, I have found it to be larger in undoubted cases of septicæmia (Experiments

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[1] Quoted from a paper in the Med. Record of August 18, 1883, by Dr. C. P. Russell.

[2] Quoted from a recent work by the present writer: Bacteria. Wm. Wood & Co., 1883.

6 and 7), produced by the injection of putrid urine and of my own saliva, than in other cases in which a solution of fish-gelatine, or of water, inoculated with organisms from swamp-mud, was the material injected (Experiments 9, 15). In rabbit No. 8, which received three successive injections (Experiments 8, 10, and 19) of swamp culture-solutions, and finally succumbed to an injection of water containing surface-mud from the gutter in front of my laboratory, the spleen was only $\frac{1}{\text{[illegible]}}$ part of the weight of the body, while in rabbit No. 7 (Experiment No. 7), in which my own saliva was injected, the proportion was $\frac{1}{518}$. This proportion seems to depend to a great extent upon the age of the animal, being greater in young rabbits.

Since writing the above I have examined the spleens of a large number of rabbits the victims of septicæmia (see "Special Report to National Board of Health" in Bulletin No. 44, April 30, 1881), and I have found the greatest diversity in the size and appearance of this organ. Sometimes it presents no appreciable changes, but commonly it is more or less swollen and discolored, and this tumefaction varies greatly, both as to its amount and as to the resulting shape of the organ. Sometimes it is enlarged in all its dimensions, and at others the length is increased without a corresponding increase in breadth.

"Another characteristic sign of malarial infection is the black pigment from the blood. This sign is not alone observed in the pernicious forms. In less serious cases of the intermittent type of long duration black pigment may be found in the spleen and sometimes in the marrow of the bones. In the gravest forms of malarial fever this pigment is found in large quantity through all the circulatory system and in many of the organs."

REMARKS.—In my post-mortem examinations of rabbits which have died from the effect of subcutaneous injections, I have been in the habit of examining the blood from the cavities of the heart and from the liver and spleen as soon as these organs were removed from the body. I have never found black pigment in the blood, but have found it in abundance in the spleens of several septicæmic rabbits, in which there could be no suspicion of malarial complication.

For fuller details with reference to the writer's experiments the reader is referred to the original report. The conclusion reached is given in the following summary statement:

Among the organisms found upon the surface of swamp-mud, near New Orleans, and in the gutters within the city limits, are some which closely resemble, and perhaps are identical with, the *Bacillus malariæ* of Klebs and Tommasi-Crudeli; but there is no satisfactory evidence that these or any of the other bacterial organisms found in such situations, when injected beneath the skin of a rabbit, give rise to a malarial fever corresponding with the ordinary paludal fevers to which man is subject.

The evidence upon which Klebs and Tommasi-Crudeli have based their claim of the discovery of a *Bacillus malariæ* cannot be accepted as sufficient; (*a*) because in their experiments and in my own the temperature curve in the rabbits experimented upon has in no case exhibited a marked and distinctive paroxysmal character; (*b*) because healthy rabbits sometimes exhibit diurnal variations of temperature (resulting apparently from changes in the external temperature) as marked as those shown in their charts; (*c*) because changes in the spleen such as they describe are not evidence of death from malarial fever, inasmuch as similar changes occur in the spleens of rabbits dead from septicæmia produced by the subcutaneous injection of human saliva; (*d*) because the presence of dark-colored pigment in the spleen of a rabbit cannot be taken as evidence of death from malarial fever, inasmuch as this is frequently found in the spleens of septicæmic rabbits.

While, however, the evidence upon which Klebs and Tommasi-Crudeli have based their claim to a discovery is not satisfactory, and their conclusions are shown not to be well founded, there is nothing in my researches to indicate that the so-called *Bacillus malariæ*, or some other of the minute organisms associated with it, is not the active agent in the causation of malarial fevers in man. On the other hand, there are many circumstances in favor of the hypothesis that the etiology of these fevers is connected, directly or indirectly, with the presence of these organisms or their germs in the air and water of malarial localities.

Since the publication of the report above referred to the belief that the *Bacillus malariæ* is the true cause of malarial fevers has received considerable support from observations made in Rome, under the direction of Tommasi-Crudeli, by Marchiafava, Cuboni, Peroncito, Ceri, and others.

We do not feel prepared to estimate the value of this evidence in detail, but will, in a general way, give our reasons for considering it in a spirit of scientific scepticism, and for demanding substantial confirmation from other parts of the world where malarial fevers prevail, and especially in our own country, where malaria is so well known by its effects, and where the *Bacillus malariæ* should be easily found if it is constantly present in the blood during the cold stage of intermittents, as has been claimed by some of the Roman observers.

In order to present to our readers a fair statement of the observations which are supposed to confirm this discovery of Klebs and Tommasi-Crudeli, we quote from an editorial in the *Medical News* of Philadelphia, in which this evidence is stated very concisely.[1]

> Following Klebs and Tommasi-Crudeli, Marchiafava and Cuboni, in Italy,[2] studied the blood of men ill with malaria. In this they found spores and bacilli which they declared to be identical with those described by the former. *The spores included in the white blood-corpuscles were sometimes so numerous as to seem to fill them completely.* Similar studies on malarial patients by Lanzi, and again by Peroncito, led to the same conclusions.
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> Succeeding these, Marchand published in Virchow's "Archiv"[3] some observations really made in 1876, whence he concluded that there exists in the blood, in the cold stage of intermittent fever, mobile and flexible rods, presenting slight swellings at their ends, and sometimes also at the middle. These end-swellings he thought also might be of the nature of spores.
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> More recent still are the elaborate experiments of Professor Ceri, of Camerino, Italy, published in the "Archiv für experimentelle Pathologie,"[4] These consisted of culture-experiments with organisms found in malarial and other soils, of experiments on animals, and culture-experiments with quinine. They resulted in proving that the spores could be cultivated—Ceri applying the term *natural germs* to those found in the atmosphere and soil, and *artificial germs* to those which result from their culture; that animals could be infected by their injection into the blood, though to a less degree by the cultivated than by the natural germs, the former growing weaker in successive generations; and that the infecting properties could be retarded by the application of heat to culture-fluids, and the introduction of quinine into them, certain degrees of the former and strengths (1 to 800) of the latter making the culture of the spores impossible, and arresting the putrid fermentation induced by them. The practical application of these facts is self-evident.
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> Finally, the opportunity has recently been presented to Dr. Franz Ziehl to test these results clinically in three typical cases of malaria, in all of which the spleen was enlarged. In all three the bacilli above described were found in the blood taken from any part of the body by the prick of a needle, and examined in the fresh state, or dried in a thin layer upon a cover-glass, by simply passing the latter over a flame. These have been preserved by Dr. Ziehl for three months without undergoing any change.
>
> The bacilli thus observed were of different lengths, but usually were from one-fourth to the entire diameter of a red corpuscle. The majority of those measured were about 4 micro-millimetres long and .7 broad. Their ends were swollen and roundish.

We remark, (*a*) that the first confirmation reported by Marchiafava and Cuboni related to the finding of bacilli and spores, *post mortem*, in the blood of patients dead from *pernicious* fever. Our observations lead us to believe that no great significance can be attached to the finding of bacterial organisms *post mortem* in the blood and tissues, especially in warm climates, unless the examination is made immediately after death. And even then we must bear in mind the possibility that they may have migrated to the blood from the intestine during the last hours of life, when the circulation is feeble and the vital resistance of cells intervening between the lumen of the intestine and its capillary vessels very much reduced.

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[1] Vol xlii., No. 2, p 41, January 13, 1883.
[2] Archiv für experimentelle Pathologie, vol. xiii.
[3] Vol. lxxxviii., p. 104, April, 1882.
[4] Vols. xv. and xvi., 1882.

(*b*) The writer's observations lead him to be very cautious in accepting evidence relating to the discovery of organisms in the blood, when these are few in number and require diligent search for their demonstration; for the possibilities of accidental contamination or of mistake in observation are very great.

(*c*) Fat-granules are found in the white corpuscles of the blood of yellow fever—which disease resembles the pernicious malarial fevers in many particulars—which bear so strong a resemblance to the spores of bacilli that a mistake might easily be made.[1] Several of the observers mention that spores were found "included in the white blood-corpuscles."

(*d*) The spores of bacilli are formed in the interior of rods and in *Bacillus malariæ* but two or three spores are formed in a single segment. How is it then that they are so numerous in the white corpuscles, when there is no mention of rods being found in the same situation?

(*e*) The writer has many times examined carefully the blood of malarial fever patients with a one-eighteenth inch oil-immersion objective (of Zeiss) and has not been successful in finding either rods or spores. But few of these examinations have, however, been made during the chill, and the blood has not been drawn directly from the spleen; these observations are therefore to be considered as incomplete, and if opportunity offers will be supplemented by more extended microscopical researches.

(*f*) While the researches of Professor Ceri relating to the germicide power of quinine are extremely interesting and important, there are many circumstances connected with its curative action in malarial diseases which cannot be reconciled with the view that this depends upon its power to destroy or arrest the development of parasitic micro-organisms in the blood—*e.g.*, the fact that it loses its curative power to a great extent in individuals who have become habituated to its physiological effects; the fact that small doses cure mild cases, and that large doses are required in the congestive forms of fever due to vaso-motor paralysis, etc., etc.

Finally we have to record the discovery by Laveran,[2] in 1881, of quite a different parasite, believed by him to be the veritable malarial germ, and named *Oscillaria malariæ*.

According to this observer, there are found in the blood of patients attacked with malarial fever pigmented parasitic elements, which present themselves under three principal aspects. This parasite is said to be a kind of animalcule which exists at first in an encysted state. In the blood these organisms present themselves as motionless, cylindrical, curved bodies, which are pointed and transparent and have a pigment spot; also as cylindrical bodies, about the diameter of a red blood corpuscle, showing active movements and containing in their interior numerous pigment granules. The movements of these bodies are due to the action of elongated filaments attached to their circumference—flagella. A third form in which these parasites present themselves in the blood is as motionless, spherical, or irregular-shaped bodies containing dark red, rounded, pigment grains. These bodies have no nucleus, and do not stain with carmine; they appear to be the ultimate stage of development of the above.

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[1] See heliotype plate showing these granules in yellow fever blood, in the writer's recent work on Bacteria. Wm Wood & Co, New York, 1883, Plate xii.

[2] A. Laveran, Surgeon Major, First Class: Nature parasitaire des accidents de l'impaludisme, etc. Paris, 1881. 104 pp., 2 pl., 8vo.

The blood also contains free pigment granules, pigmented leucocytes, and vacuolated red corpuscles which contain pigment granules.

These parasitic elements have only been found in the blood of persons sick with malarial fever, and they disappear when quinine is administered. They are of the same nature as the pigmented bodies which exist in great numbers in the vessels and organs of patients dead with pernicious fever, which have been described as melanotic leucocytes. Laveran, at the time his report was published, had found these bodies in 180 out of 192 persons examined in Algeria and in Tunis, who were affected with various symptoms of malarial poisoning.

The presence of the parasite described by Laveran in the blood of persons suffering from malarial diseases is confirmed by Richard,[1] who has studied the subject at Phillipeville, France, where malarial diseases abound. This author has invariably found the parasite of Laveran in the blood of malarial fever patients, and has never seen it in the blood of persons suffering from other diseases. He finds that its special habitat in the blood is the red corpuscles, in which it develops and which it leaves when it has reached maturity. During the attack of fever many blood-globules are seen which possess a small, perfectly round spot. Otherwise they preserve their normal appearance; they are simply, so to speak, stung (*piqués*). Besides these globules are others in which the evolution of the microbe is more advanced. The clear spot is larger and is surrounded by fine black granules. The surrounding hæmoglobin forms a ring which decreases as the parasite augments in volume. After a time only a narrow colorless zone remains at the margin. This corresponds with the body No. 2 of Laveran, "having about the dimensions of a red corpuscle and enclosing an elegant collarette of black granules." This collarette is the microbe which has arrived at its perfect state, and which is provided with one or several slender prolongations, measuring 25 micro-millimetres or more in length. Richard has several times seen the fully developed parasite emerge from its "shell"—the remnant of the invaded red corpuscle—to which it may remain attached, and which can only be seen with great difficulty. Sometimes only the motile filaments penetrate the envelope in which the body of the parasite remains enclosed. In both cases the filament is seen to undergo active movements, and when its extremity is caught in the fibrinous reticulum the body itself oscillates. This movement may last for an hour. Usually, however, no movement is observed, and the corpuscles containing very small parasites never move. The infected corpuscles become disorganized, the pigmentary collarette is broken down, and a grayish mass enclosing some black granules remains. The pigment granules when set free are rapidly picked up by the leucocytes; the melaniferous leucocytes are therefore epiphenomena. M. Laveran has also described elongated bodies which Richard has often seen in the blood of old cases and believes to be red corpuscles containing parasites which have become deformed by pressure in the smallest capillaries, in which the parasites are arrested in their development.

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[1] M. Richard: Sur le parasite de la malaria, Compt. rend. Acad. d. sc., Par., 1882, xciv., p 496.

Acetic acid added to a drop of blood does not destroy the parasites, but destroys the normal blood-globules, so that by treatment with this reagent the parasites are more readily found when few in number.

These observations of Laveran and of Richard are entitled to equal consideration with those of the Italian observers who find the *Bacillus malariæ* in the blood of their malarial fever cases in the vicinity of Rome.

We cannot doubt that a true account has been given in both cases of what the observers believe they have seen. But there is a wide field for doubt as to the deductions made from the various observations recorded; for in microscopical studies of the blood made with high powers there is a great liability to error and to misinterpretation of what is seen. We may question, for example, whether the belief of Laveran and Richard that the appearances noted by them are due to parasitic invasion of the blood-corpuscles is well founded, without calling in question the accuracy of their observations.

As the Italian observers make no mention of the *Oscillaria malariæ* of Laveran, and as the French observers seem not to have encountered the *Bacillus malariæ*, each series of observations is, in a negative way, opposed to the other. It is evident, therefore, that physicians in this country who wish to know the exact truth as regards the nature of malaria will do well to investigate for themselves, or at least to encourage investigations at home by those who seem fitted by education and inclination to undertake them.

The practical object which the writer has had in view in devoting so much space to these various claims to the discovery of the precise nature of malaria has been to direct future inquiry; to indicate the difficulties attending such investigations; and especially to point out the great liability to make pseudo-discoveries, and consequently the importance of special scientific training and a truly conservative spirit on the part of the investigator.

With a view to further direct the course of experimental inquiry, the author ventures to indulge in the following remarks.

The circumstances heretofore detailed (Chapter II.) relating to the production of malaria give very strong support to the belief that the poison which is produced in the soil—in the presence of organic matter, ground-water, and ground-air, and under the influence of an elevated temperature—is a living organism or a chemical product evolved during the active growth of such an organism. This being admitted, several possibilities present themselves:

(*a*) Malarial poisoning may be an *intoxication* resulting from the respiration of an atmosphere containing a toxic agent produced by living organisms in the soil.

(*b*) It may be an *infection* resulting from the respiration of an atmosphere charged with malarial germs, born in the soil, which enter the circulation and multiply in the blood, or in special organs, and produce *directly* the morbid phenomena which characterize malarial diseases.

(*c*) Malarial intoxication may result from infection by malarial germs, born in the soil, which multiply within the body of the infected individual and there produce a toxic chemical agent to which the morbid phenomena are due. In this case it is not necessary to suppose that the malarial parasite invades the blood. It may remain in the alimentary canal, where it would find abundant pabulum in the food ingested, and where the poisonous products evolved during its active growth would find ready access, by absorption, to the circulating fluid.

We confess that either the first or the third of these several hypotheses seems to us to have more in its favor than the second, which, however, is that which has of late received the most consideration, and is that advocated by Tommasi-Crudeli and the believers in his *Bacillus malariæ*.

This author explains the phenomena of a malarial paroxysm as follows:

"Tommasi-Crudeli thinks that the rigors may be produced by the irritation of the vaso-motor nerves by the bacilli in the circulation, that the febrile attack is the result of the discharge of the bacilli from their special *nidus* in great quantities, and that their development and disintegration are accelerated by the high temperature, abundant nourishment, and oxygen of the blood."[1]

The truth of this view would, of course, receive strong support if observers in various parts of the world were able to verify the statement of the Italian observers as to the presence of bacilli in the blood in large numbers during the cold stage of ague. But in the absence of satisfactory verification of the alleged fact, we venture to suggest certain objections which seem to weigh against the truth of the hypothesis.

We remark, first, that the paroxysm of intermittent fever seems at times to be rather an accident or sequela of malarial poisoning than a direct result of the action of the poison, for it is frequently induced by secondary causes, such as chill, fatigue, etc., and it often does not occur at all when there is ample evidence that the general health is seriously impaired by the direct action of malaria.

Second, the effects seem to vary with the dose. After exposure to the poison in a concentrated form—*e.g.*, in a tropical swamp at night—the symptoms of poisoning may be quickly developed and are often most intense in kind. When, however, the dose is smaller but frequently repeated, as when one habitually lives in a malarious atmosphere, we may have symptoms of chronic poisoning, and this perhaps without paroxysmal febrile attacks. In the germ diseases, demonstrated to be such, on the other hand —*e.g.*, in anthrax or fowl cholera—a minute quantity of material containing germs is as efficient as a larger amount; for the capacity of these germs for rapid self-multiplication makes the question of quantity one of little importance.

And in infectious germ diseases, transmissible by inoculation from one animal to another, as Klebs and Tommasi-Crudeli claim that malarial fevers may be, the evolution of the disease after the introduction of germs undergoes a regular course, and if the animal survives the acute attack which results, it in future enjoys a certain immunity from the disease in question. In malarial poisoning, however, not only is it generally recognized that the gravity of the symptoms depends upon the quantity of the poison introduced, but also that no immunity results from repeated attacks.

Again, we are not prepared to admit the force of the argument drawn from Professor Ceri's experiments relating to the germicide power of quinine.[2] For it is difficult to understand how a few germs, just enough to produce a periodic neuralgia, for example, or a mild tertian ague, should be killed by moderate doses of quinine or of arsenic,[1] while in a case of congestive intermittent heroic doses of quinine are necessary to save life. Our experiments lead us to believe that a few germs in a large quantity of fluid—the entire quantity of blood in the supposed case—require as large a percentage of the germicide agent for their destruction as a great many germs in the same quantity of fluid. And when a culture-fluid is suitable for the development of germs at all, they pervade it throughout. It seems to us also that clinical facts require an explanation of the *antiperiodic* action of quinine upon some other hypothesis than that which supposes that it destroys or prevents the development of germs in the blood. We have other germicide agents more potent than quinine, which nevertheless do not exhibit equal power to neutralize the effects of malaria. According to Arloing, Cornevin, and Thomas, a ten per cent. solution of sulphate of quinine has no action upon the bacterium of symptomatic anthrax (presumably because it contains spores); and Koch finds that it takes ten days for a one per cent. solution of quinine, *dissolved with muriatic acid*, to destroy the spores of bacilli.

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[1] Fayrer, op. cit., p. 28.

[2] Binz concluded from his researches that twelve to fifteen grammes of quinine in twenty-four hours would be required to kill inferior organisms in the blood. Vulpian arrived at the conclusion that thirty grammes of chlor-hydrate of quinine in twenty-four hours would be required. Bochefontaine finds from his experiments that at least one part in eight hundred would be required to kill vibrioniens in the blood, equal to seventeen grammes. (Bochefontaine: "Experiments Relative to the Action of Quinine upon the Vibrioniens." Arch. de physiol. norm. et path., Par., 1873, p. 389.)

A dose of ten grains of quinine if absorbed at once and retained in the blood would not constitute, in an adult weighing one hundred and sixty pounds, $\frac{1}{150}$ part of one per cent. of the entire mass of blood. Now if infection in malarial localities results from the respiration of an atmosphere containing bacilli and spores, how shall we account for the prophylactic value of small doses of quinine taken once daily? On the other hand, if these doses do destroy or prevent the development of spores, how shall we account for relapses after removal to a healthy locality and after treatment with full doses of quinine, or for those obstinate cases which resist the curative action of this remedy? Does the *Bacillus malariæ* become habituated in certain individuals to the antidote?

Notwithstanding what has been said, we admit that there are circumstances relating to the malarial fevers which give support to the belief that the malarial poison is reproduced within the body. The recurrence of attacks at a remote interval after exposure especially favors this belief. Nor are we disposed to deny the possibility that the beneficial action of quinine is due, in part at least, to its power to restrain the development of micro-organisms. But it seems to us far more probable that this action is exercised in the intestine rather than in the blood; and we cannot believe that this is a complete explanation of the *modus operandi* of quinine in the cure of malarial diseases.

Our third hypothesis (*c*) seems to be worthy of the special attention of future investigators. The human intestine has a microscopic fauna and flora almost equal to that of a city gutter. The larger animal parasites of this internal sewer are well known, but the bacterial flora has been very imperfectly studied. It is now generally known, however, that the mouth and the intestine in healthy persons is habitually inhabited by a variety of bacterial organisms.[2]

The human mouth, with its uniform temperature, free access of oxygen, and constant supply of pabulum—the salivary secretions—is an admirable culture apparatus. Here, consequently, there is forever going on a

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[1] According to Dougall, "arsenious acid has less germicide power than sulphate of iron, which itself does not stand very high among the metallic salts." (Parkes, in Report English Army Med. Dept., 1870, Appendix, p. 248.)

[2] See the writer's paper on "Bacteria in Healthy Individuals," in Studies from the Biological Laboratory, Johns Hopkins University, Balt. Vol. II., No. 2, 177–181, 3 pl.

"struggle for existence" among a multitude of minute parasites, some of which are habitually the commensals of man. These are harmless, and may even play an important physiological rôle in the human economy. The same may be said of the bacteria which habitually infest the human intestine. The smallest smear of fecal matter spread upon a thin glass cover, and stained with an aniline dye, will be seen under the microscope to contain a multitude of bacteria of various forms. Evidently these are harmless, and possibly, as heretofore suggested, they may be useful and even necessary agents in the intestinal digestion of the coarser portions of ingested material which pass through the pylorus in a condition unfit for assimilation. However this may be, it is not difficult to believe that other species, whose normal habitat is external to the body—in swamps or elsewhere—when introduced into the human intestine, as they often must be in considerable numbers, may give rise to special kinds of fermentation and to the production of special products which are not harmless. We may suppose that the malarial germ acts in this way. Whether this suggestion has any value can only be determined by extended and carefully conducted investigations.

The argument drawn from Professor Ceri's experiments relating to the power of quinine to arrest the development of bacteria is more forcible under this hypothesis than when we suppose the blood itself to be invaded by the malarial parasite. It also accounts for the generally recognized value of evacuants in the treatment of malarial fevers. Very many practitioners insist upon the importance of administering one or more doses of a *mercurial* cathartic at the outset, and an occasional repetition of the same during the progress of a case of malarial fever. The beneficial action of such medication would be explained, under the hypothesis at present under consideration, by the cleansing of the intestine of the pathogenic organisms and of the pabulum for their development, and also by the germicide power of the mercurial.

The value attached by the older practitioners in this country to the administration of occasional full doses of calomel in malarial diseases is well known. Their experience, gained empirically, is in accord with the hypothesis under consideration, and with the results of modern researches as to the *modus operandi* of this remedy. Thus Wassilieff,[1] in a recent paper relating to the "Influence of Calomel on Fermentation and the Life of Micro-Organisms," concludes that "the therapeutic virtues of calomel are to be ascribed to its antiseptic and disinfectant properties." This hypothesis (*c*) does not exclude the first (*a*), which supposes that malaria is a chemical poison produced in the soil by the vital activity of micro-organisms, but it involves the additional hypothesis that the same micro-organisms may multiply within the alimentary canal and there produce the same poison.

The belief that malarial poisoning is simply an intoxication, and not an infection by living germs, is sustained by M. Colin. This author says:

> It is evident that malaria is a poison and not a virus; that it therefore acts the more quickly and the more rapidly as this has been stronger. We know how different is the action of a virus which, in addition to the fact that its influence is independent of quantity, confers immunity against a second attack; while the best condition in which to have an intermittent fever is to have already suffered an attack.[2]

If we accept this view we must look upon the febrile paroxysms which often occur long after exposure as secondary results of malarial poisoning.

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[1] Ztschr. f. physiol. Chem., Strassb., vi., 112–114.

[2] Op. cit., p. 118.

It is well known that these are often induced, months after removal to a healthy locality, by exposure to cold, indiscretions in diet, etc., in persons who have previously resided in a malarial region; and it not infrequently happens that these characteristic intermittent paroxysms occur for the first time after removal from the place where the exposure occurred.

The view that the primary action of the malarial poison is upon the nervous centres, and especially upon the sympathetic ganglia, and that the paroxysms are due to disturbance of innervation rather than to the presence of a ferment in the blood, has been advocated by numerous authors.

Periodicity from this point of view, is a phenomenon relating to the nervous system and not resulting from the periodic regeneration of the poison.

In support of this we have the fact that exposure under the same circumstances may cause in one person a quotidian, in another a tertian, and in a third a quartan ague. If this is not due to individual peculiarities, we must suppose that there are as many varieties of malaria—or of *Bacillus malariæ*—as there are types of malarial fever.

As neither the researches which have been made nor the speculations in which we have indulged have brought us to the point of answering in a definite manner the question, What is malaria? we are reduced to the necessity of concluding this chapter with an acknowledgment of ignorance as to the real nature of this widely distributed poison.

CHAPTER IV.

GENERAL EFFECTS OF MALARIA.

THE effects of exposure to malaria are manifested by persons of all ages and of all nationalities; but marked differences exist both as to race and as to individual susceptibility.

INFLUENCE OF RACE.—Those races which from time immemorial have inhabited the most intensely malarious regions enjoy a certain immunity, as compared with those from regions more remote from the equator, where the malarial poison is produced less abundantly or not at all. Hence it may be said in general that the dark-skinned races are less susceptible than those of fair complexion. It does not follow, however, and so far as the writer is aware is not true, that blonds are more susceptible than brunettes of the same race. There is no reason to suppose that the black skin of the negro affords him any protection from malaria, any more than his curly hair. But as he belongs to a race which has from remote ages inhabited tropical and therefore malarious regions, and as observation shows that individual differences in susceptibility exist, the laws of natural selection must have inevitably come into play, and the tendency is constantly in the direction of race immunity. This is doubtless the true explanation of the less degree of susceptibility of the negro, and is not at all opposed by the fact that individual susceptibility increases with exposure. Indeed, this circumstance intensifies the effect of slight differences in individual susceptibility. For the more susceptible person will not only be soonest attacked, but each attack helps to establish a predisposition to future attacks. Extinction of the most susceptible and survival of the fittest is further promoted by the readiness with which such individuals fall victims to other endemic or epidemic diseases.

The general statement that the races inhabiting intensely malarious regions enjoy a comparative immunity from malarial poisoning is not sustained by the mortality statistics relating to white and colored troops in the army of the United States during the civil war, or by a comparison of the mortality among whites and natives in India. But, as we shall show, the fact is as stated, and the statistics are misleading, unless certain circumstances which do not appear in the mortality reports are considered in connection with them.

Fayrer says: "Contrary to what might be expected, natives suffer more than Europeans in India, no doubt on account of the unfavorable conditions under which they live. The Europeans are, for the most part, well housed and fed and guarded against insanitary influences. The natives are much exposed to the action of malaria, poorly fed and badly housed."[1]

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[1] Op. cit., p. 53.

The same author says, on another page: "The natives of India suffer greatly, but it would appear that the negroes on some parts of the coast of Guinea acquire a tolerance which has been referred, possibly without sufficient reason, to the color of the skin. There are certain tribes in the Terai and other forest districts of India which acquire some immunity; the non-Aryan races, such as inhabit Assam, suffer, it is said, to a greater extent from malarial disease than the Aryans in the same province. The Tharoos live where it would be death to others, but even they are not altogether exempt" (p. 41).

The difference in race susceptibility is often covered up in statistical tables by the extra exposure of the colored races, and by the grouping of cases having a different etiology with those of malarial origin under the heading "malarial fevers."

Thus if we take the total amount of sickness and mortality from malarial diseases in the armies of the United States during the civil war, we shall find that it is greater for the colored than for the white troops. This is mainly due to the fact that the colored troops were enlisted and kept in southern latitudes, and were selected to garrison posts located in malarious regions. When we compare, however, white and colored troops serving together, we shall find the advantage quite decidedly in favor of the negro. This is shown by the following table, which exhibits the absolute and relative number of cases of periodic fever occurring among the white and colored troops serving in the Department of Texas, during the year ending June 30, 1883. I am indebted for this table to Col. Jos. R. Smith, Surgeon U.S.A., Medical Director Department of Texas.

Table exhibiting Prevalence of Periodic Fevers at Different Posts in the Department of Texas.

POSTS.		Mean strength.	Remittent fever.	Quotidian intermittent fever.	Tertian intermittent fever.	Quartan intermittent fever.	Total periodic fevers.	All cases of disease, etc., reported.	Per cent. of periodic fevers to all kinds.
Fort Brown......	White.	195	60	117	2	..	179	540	33.15
Fort Clark.....	White.	507	17	183	23	..	223	787	28.46
	Colored.	34	..	...	..	..	...	18	....
Fort Concho....	White.	230	16	2	1	..	39	430	9.07
	Colored.	130	..	1	..	..	1	191	0.52
Fort Davis.....	White.	79	..	19	..	..	19	123	15.45
	Colored.	486	5	74	7	..	86	1,216	7.07
Fort Duncan.....	White.	122	37	8	7	..	52	224	23.21
Fort McIntosh....	White.	135	1	23	9	..	33	274	12.04
Fort McKaroll....	White.	59	..	8	..	..	8	72	11.11
Fort Ringgold....	White.	170	..	74	2	..	76	370	20.54
Fort Stockton....	Colored.	104	3	1	..	2	6	58	10.34
San Antonio......	White.	247	16	11	27	..	54	377	14.32
Total white............		1,744	147	465	71	..	683	3,197	21.36
Total colored...........		754	8	76	7	2	93	1,483	6.27
Total................		2,498	155	541	78	2	776	4,680	16.58

Dr. Smith remarks as follows in a letter accompanying this table:

"You will see that the percentage of these diseases was more than three times as great among the white troops as among the colored troops.

Where white and colored troops were serving side by side at the same post, almost an equally great difference is observed. During the year previous, viz., that ending June 30, 1882, the percentage of cases of periodic fever occurring among the white troops was more than *four* times the percentage of cases occurring among the colored troops."

It is generally, and we believe correctly, stated that negroes born in Africa are less susceptible to malaria than are their descendants born in more temperate and less malarious regions. In support of this statement M. Colin refers to the following facts reported by Dr. M'William in his "Medical History of the Expedition to the Niger during the Years 1841–42" (London, 1843).

The expedition consisted of three vessels, the Albert, Wilberforce, and Soudan. The crews were made up of (1) English sailors; (2) black sailors recruited in England; and (3) black sailors recruited on the west coast of Africa. The vessels remained for forty-five days in the river. The sickness and mortality from *fever* was as follows:

	Total number.	Taken sick.	Died.
White sailors	145	130	40
Black sailors recruited in England	25	11	..
Black sailors recruited on the coast of Africa	133	..	..

These figures are given by M. Colin as evidence of the comparative immunity of the colored race from malarial fevers. The absolute immunity of one hundred and thirty-three negroes from the coast of Africa, when nearly ninety per cent. of the white sailors were taken sick and more than twenty per cent. died, arouses a suspicion, however, that the *malarial* fever in this case was yellow fever. In this disease one attack protects from subsequent attacks; and as yellow fever is endemic on the west coast of Africa, it seems highly probable that this is the true explanation of the remarkable difference in susceptibility shown in this instance. As in the case of malarial fevers properly so-called, the negro race enjoys a comparative immunity from yellow fever, but this is manifested by the mild nature of the attack and small mortality rather than by complete exemption from the disease, except as a result of a previous attack.

Bartlett, in commenting upon this fever, says: "Dr. M'William's description of the disease is very incomplete and unsatisfactory. It was evidently remittent, many of the cases being congestive or malignant. There was no case of black vomit; and, indeed, there seems to have been little or no resemblance between it and yellow fever, although Dr. M'William not only makes no distinction between the two diseases, but evidently confounds them."

A comparative statement of the mortality from malarial diseases among the white and colored troops in the entire army of the United States for three years is given in Circular No. 4, Surgeon-General's Office, Washington, D. C., December 5, 1870 (Table B). This was as follows:

Ratio per 1,000 *of Mortality from Malarial Diseases in the U. S. Army.*

	1868.	1869.	1870.
White	94.20	140.67	72.99
Colored	74.62	15.62	38.46

Here the difference in favor of the colored troops is not very decided in 1868, and is less than one-half in 1870. But in 1869 the mortality among white troops from malarial diseases is nine-fold that among the colored troops. How shall we account for this notable difference in different years? A consideration of the figures relating to mortality from continued fevers for the same years, taken in connection with other facts referred to in the Introduction to this volume, leads us to suspect that this difference is due, in part at least, to the fact that the colored troops were, in 1868 and in 1870, brought more within the influence of the poison of enteric fever, to which they are especially susceptible, and that a considerable proportion of the mortality which appears under the heading malarial fevers is due to those "continued malarial fevers" which are improperly called malarial.

Ratio per 1,000 *of Mortality from Continued Fevers in the U. S. Army.*

	1868.	1869.	1870.
White	126.08	137.61	65.69
Colored	126.86	46.86	115.38

In 1868, when the mortality from continued fevers was about the same, the mortality from malarial fevers among the colored troops was but little less than that among the white troops; while in 1869, when the white troops suffered severely from continued fevers and the colored troops to only one-third the extent, we find a most striking difference—one to nine—in the mortality from malarial fevers. This difference cannot be ascribed to a less degree of exposure to malarial influences, for the white troops have constantly had the advantage in this respect, as they have, as a general rule, occupied the more northerly stations.

This view receives further support from a consideration of the statistical data contained in the first medical volume of "The Medical and Surgical History of the War of the Rebellion." From this source we obtain the following table, which has been computed from the returns for three years. For the white troops, from June 30, 1862, to July 1, 1865; mean strength, 660,291. For the colored troops, from June 30, 1863, to July 1, 1866; mean strength, 63,645.

Annual Rate per 100 *of Sickness and Mortality from Continued and Malarial Fevers, in the Armies of the United States during the War of the Rebellion.*[1]

	Ratio of cases to mean strength.		Ratio of deaths to mean strength.		Ratio of deaths to cases.	
	White.	Colored.	White.	Colored.	White.	Colored.
Typhoid	2.62	2.14	1.05	1.19	39.89	53.24
Typho-malarial	2.43	3.94	0.19	1.01	7.08	17.28
Remittent	11.62	16.05	0.16	0.52	1.39	3.27
Intermittent	36.54	62.77	0.04	0.06	0.18	0.10
Congestive intermittent	0.53	1.32	0.14	0.36	26.23	31.30

From this table we learn that the colored race is more susceptible to the typhoid poison than the white, the ratio of cases to mean strength being somewhat greater when we add together the cases diagnosed as "typhoid" and "typho-malarial." This greater susceptibility is shown in a more decided manner by the excessive mortality among the colored troops from this class of fevers.

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[1] In this table the ratio is obtained from the mean strength and total number of cases during the whole period (three years), the total ratio being divided by three for the annual ratio.

If we turn now to the mortality from intermittent fever, it is found to be considerably less (0.18 white, 0.10 colored) when we compare the number of deaths with the number of cases, although the exposure of the negro troops was much greater than that of the white troops, as is shown by the considerably larger percentage of cases in a less susceptible race (intermittent fever, 36.54 white, 62.77 colored). This exposure to malaria in a more intense form is also shown by the larger number of cases of congestive intermittent among the colored troops (0.53 white, 1.32 colored). We find also that the number of cases of remittent fever was greater among the colored troops by nearly one-half. But on turning to the column showing the ratio of deaths to cases, we are surprised to find that in the least susceptible race the mortality from fevers diagnosed as "remittent" is nearly two and a half times greater than among the more susceptible white troops. Our explanation of this apparent contradiction is that a certain proportion of these fatal cases of "remittent fever" belong properly with the group of typhoid fevers, which, as we have seen, are especially fatal to the colored race.

INFLUENCE OF AGE.—No age is exempt from the effects of malarial poisoning, and if the aged and the very young enjoy an apparent immunity, it is probable that this results from a less degree of exposure, as they remain at home and are seldom exposed to the "night air," which is so generally recognized as especially dangerous in malarious regions. According to Wunderlich, children suffer most frequently from intermittent bowel troubles.[1] Cleghorn says that malignant tertians are most common among adults and aged persons. Dr. Charles Parry says that children are rarely affected with congestive fever; he has never seen a case in an individual under twenty years of age. Dr. Wharton, of Mississippi, says that children under ten are comparatively free from attacks of congestive fever. On the other hand, Dr. Lewis, of Mobile, thinks the liability to congestive fever is alike at all ages, and that greater frequency among adults is due entirely to greater exposure.[2] The special effects of malaria upon children have been referred to by numerous authors, but there can be little question that the *kind of malaria* which produces the effects described differs essentially from that special poison which we recognize by this name. Thus, in a recent paper by Dr Holt, of New York, we learn that "malaria in children" is very common in that city. But we read in the report of his paper, which is at hand,[3] that "periodicity could not be relied upon to any great extent in diagnosis." In the discussion upon this paper, which was read before the New York County Medical Society, Dr. J. Lewis Smith remarked that he had seen a great many cases in private practice resembling those described by Dr. Holt. "He thought cases of malaria might properly be divided into two classes—those which were due to marsh miasm and those which were of a remittent character and due to a polluted soil or sewer-gas. He believed that the majority of these cases apparently of malaria in children were really cases of typhoid fever.

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[1] Hertz, in Ziemssen, vol. ii., p. 573.
[2] Bartlett, op. cit., p. 345.
[3] Med. Times, Phila., Dec. 16, 1882, p. 208.

"Dr. John C. Peters said that there was great difficulty in diagnosing malarial fevers in children under five years of age. Certainly some cases of ordinary remittent fever due to sewer-gas poisoning simulated malarial fever closely. He knew of several cases in which the paroxysms were distinctly intermittent in type, and the only possibility of malarial poisoning was through sewer-gas."

INFLUENCE OF SEX.—Statistical tables show that males are more subject to malarial fevers than females. This is undoubtedly due to the increased exposure which results from the different nature of their usual occupations—laborers, farmers, soldiers, etc. The fact that pregnant and puerperal women seem sometimes to have a certain immunity is probably due to the circumstance that their condition requires them to keep within doors. According to Ritter, this apparent immunity only exists during the last months of pregnancy.

The truth in regard to puerperal women seems to be that they are especially susceptible to the influence of malaria as a result of the loss of blood and exhaustion immediately following confinement. It must be remembered, also, that they are liable to suffer from an intermittent or remittent septic fever, due to the absorption of septic products formed in the interior of the uterus. This, no doubt, is sometimes improperly ascribed to the action of malaria.

SUSCEPTIBILITY RESULTING FROM PREVIOUS ATTACKS.—However closely the specific continued fevers may simulate the malarial fevers in their clinical history, there is one broad line of distinction between these two classes of disease. A single attack, however mild, of the former usually protects the individual from future attacks; whereas an attack of a truly malarial fever predisposes to future attacks. This statement is based upon the observations of physicians in all parts of the world, and the latter clause, at least, is so generally recognized as true of the typical malarial fevers—intermittents—that we think it safe to conclude that any febrile attack which confers immunity from subsequent attacks is not malarial. This being the case, we must suppose that the attacks of "acclimating fevers" which occur so commonly among strangers upon their arrival in tropical regions are improperly ascribed to malaria; for if they were truly malarial we should expect that continued exposure under the same conditions as gave rise to the first attack would produce other attacks of the same kind, whereas the very name, "acclimating fever," shows that a single attack is considered protective.

The fact that continued exposure to malaria only intensifies the effects of the poison, and that no acclimation is possible in the sense of its affording protection against this particular poison, is well set forth by M. Colin, who says:

> If some of our French garrisons in hot countries give but a relatively small ratio of mortality, it will not do to conclude that residence in these localities is innocuous to men from the North, or that colonies can be established with facility; a great part of the success in these places comes from the short sojourn of the same regiments. At Mayotte, for example; at Madagascar, where one cannot remain longer than six months without danger; in the Antilles, where the sojourn of the stranger ought not to exceed two years. One cannot invoke in favor of acclimatization in these countries the influence of habit, for one never becomes habituated to the influence of the paludal miasm. . . . Thévenot expresses the same opinion in the two following passages: "The different classes of Europeans suffer the more severely according as they have been longer subjected to the influence of malaria; the soldiers more than the sedentary merchants, these more than the sailors, and among these the merchant crews more than the military crews. . . . The mortality of the troops in Senegal seems to

augment according to the length of their sojourn, the organisms are worn out by the relapses, the maladies become chronic and irremediable; there is then no acclimatization possible for the soldier."

In Rome the same regiments remained, under the same numbers, for several years; but during this period so many men were returned to France and replaced by new-comers that the soldiers were, at the end of a certain time, almost entirely renewed.[1]

On another page M. Colin tells us that the majority of the French troops quartered in the centre of the city, or in the least unhealthy localities in the suburbs, usually escaped an attack of remittent fever during the first two years of their stay, and that out of five hundred cases of which he had made notes, three-fourths were attacked for the first time during the third year of their residence in Rome. The fact that tourists are not infrequently seized within a few weeks after their arrival is ascribed to their imprudence, which leads them to expose themselves at night, etc., and to the fatigue and excitement to which they are subjected. That strangers who are prudent resist the diluted malaria within the city limits for two years, is said to be a popular belief among the Roman people.

It is unnecessary to dwell further upon the fact that previous exposure to malaria constitutes a predisposition to be attacked by malarial diseases. The experience of our own army surgeons and of civil practitioners in malarious regions in the United States quite accords, in this particular, with that of observers in other parts of the world.

SUSCEPTIBILITY FROM OTHER CAUSES.—It may be said, in general, that any disease or injury which lowers the vital energy of an individual increases his susceptibility to the influence of malaria. Thus malarial poisoning may complicate other diseases, as in the case of so-called typho-malarial fever, or attacks of malarial fever may occur during convalescence from acute diseases, as a result of exposure to the poison in so attenuated a form that it would be inefficient to produce an attack in a healthy person.

SUSCEPTIBILITY OF THE LOWER ANIMALS.—The question of the susceptibility of the lower animals to malaria is one of extreme interest at the present time, because of the general desire to obtain an exact knowledge of the nature of this poison. The experimental investigation of this question would be greatly simplified if it were definitely proven that any one of the domestic animals available for experimental purposes is susceptible to well-marked attacks of periodic fever. Many of the older authors claimed that such susceptibility exists, and have recorded examples in support of this belief. But it is necessary to receive much of this evidence with great caution, for in some cases at least it is apparent that other diseases peculiar to the lower animals have been mistaken for malarial fevers, and some of the authors who have been quoted seem to have used the word malarial in the broad sense which has given rise to so much confusion.

If the domestic animals are subject to attacks of the typical periodic fevers, the fact should be easily verified by evidence obtained in our own country and at the present day. The writer is especially interested in this question, and will be obliged to any reader who may be able to give definite affirmative evidence from his personal observations if he will communicate to him the facts.

The following quotation, from the classical work of Dr. Watson,[2] is given as an example of the kind of evidence which has been offered in support of the susceptibility of the lower animals, but to which we can accord no scientific value. For admitting the facts, the inference that animals desert the forests and lowlands to escape malaria rather than to avoid the excessive heat or the attacks of insect pests can scarcely be considered worthy of serious attention.

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[1] Op. cit., p. 496.

[2] Practice of Physic, Am. ed., 1845, p. 453.

The late Bishop Heber, in his "Narrative of a Journey through the Upper Provinces of India," gives the following striking picture of the influence of malaria in that part of the world. It seems to be alike pestiferous to man and beast. "I asked Mr. Boulderson if it were true that the monkeys forsook these woods during the unwholesome months He answered that not the monkeys only, but everything which has the breath of life instinctively deserts them from the beginning of April to October. The tigers go up to the hills, the antelopes and wild hogs make incursions into the cultivated plain, and those persons—such as dâk-bearers or military officers—who are obliged to traverse the forest in the intervening months agree that not so much as a bird can be heard or seen in the frightful solitude."

The evidence in favor of the view that the lower animals are susceptible to malarial poisoning is summarized as follows by Professor Fleming:

The occurrence of malarial fever in animals has been often denied, but a host of observers, in every way trustworthy, have testified to its existence in nearly every part of the globe. Those to whom I can just now refer as witnesses are Carlo Ruini and Lancisi in the sixteenth and seventeenth centuries; in the eighteenth century, Kersting, Waldinger, and Veith; in this century, Damoiseau, Rodet, Liégeard, Hamont, Clichy, Blanc, Hering, Spinola, Hertwig, Dressler, Delwart, Legrain, Bertacchi, and other veterinarians of repute. Lessona, a distinguished Italian veterinary surgeon, has frequently observed it affecting horses, cattle, and dogs in Sardinia. Blaise has seen it in the same animals in Algeria; Hamont also in Egypt; Bertacchi in the Pontine Marshes; Hildreth in America affecting dogs). Dupuy and Cleghorn assert that sheep are greatly predisposed to it. Jenisch has seen it in the pig, and Czermak states that he has noticed it not only in dogs, but in monkeys also.

The attacks resemble those of paludal fever in mankind, and their duration is usually brief—from half an hour to six or seven hours after which the animal is apparently easier; though if closely observed a certain degree of *malaise* will be noted—as frequent yawning, saffron-tinted mucous membranes (this is most marked during the attack); tension of the abdomen, which is often painful on pressure in the region of the liver; often there is gastric disturbance, and in the dog, vomiting. All the types of the fever have been witnessed—quotidian, tertian, etc.

When the disease continues for some time, a cachexia appears to be developed, with localization of lesions in certain organs, the most notable of which are those of chronic congestion, particularly of the spleen, sometimes the liver, in other cases the lymphatic glands.

It is extremely difficult indeed to diagnose the presence of neuralgia in dumb animals. I have only seen it once, for certain, in a dog.

Veterinarians have long noticed that domestic animals living in malarious regions have the paludal cachexia, and that in them intermittent fever often complicates or accompanies other maladies, sometimes even occurring after operations or accidents. Anthrax or charbon was, until the discovery of the *Bacillus anthracis*, believed to be malarial. The horse-sickness of South Africa is even now believed to be malarial, as people suffer severely from intermittent or remittent fever when and where it prevails; but I am now quite convinced that it is only anthrax, as it is inoculable and I have found bacilli in the blood. The terrible "Yaswa" of Russia, which kills enormous numbers of horses, cattle, and other animals, as well as (by transmission) people, is only witnessed in malarial regions, but it also is only anthrax.

I may add that in 1861 I had several cases, among horses in North Carolina, of what I considered well-marked intermittent. I forgot to mention, in connection with the horse-sickness of South Africa, that dogs suffer in the malarial districts of that country from a disease which is evidently malarial. It is more particularly noticed in the valley of the Limpopo, and away north to the Zambesi. It is known to the Boers as the "hond-ziekte," or dog-sickness, and is very fatal. The liver appears to be the organ chiefly involved, as the mucous membranes are deep yellow in color (*geel bec*, or "yellow-mouth" of the Boers), the abdomen is enlarged, there is jaundice, constipation, and high temperature.[1]

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[1] Quoted from Fayrer, op cit., p. 47.

We venture to differ with Professor Fleming as to the etiology of this disease of dogs which he says is "evidently malarial." A similar disease in the island of Cuba has been pronounced yellow fever. We believe it to be neither one nor the other of these. If malaria can produce a fatal disease of this character in South Africa, similar results should follow exposure to the same cause in intensely malarious regions elsewhere; and if the yellow-fever poison is responsible for sporadic attacks of a similar nature in Cuba, we have a right to expect that during extended epidemics of this disease in our own country the same poison will produce a similar effect. We have, however, no satisfactory evidence that this is the case. In view of Professor Fleming's statement that anthrax was believed to be malarial by the veterinarians prior to the discovery of the *Bacillus anthracis*, we can accord but little weight to the observations of the "witnesses" named, whose testimony was recorded before the introduction of the clinical thermometer and of exact methods of diagnosis.

GENERAL EFFECTS OF MALARIAL POISONING AS SHOWN BY VITAL STATISTICS.

The following table is compiled from data contained in Circular No. 4, Surgeon-General's Office, Washington, December 5, 1870 (Table B.):

Ratio per 1,000 *of Mortality from Malarial Fevers.*

	Period.	Ratio.
United States Army	1840–54	108.02
" " "	1855–59	61.08
" " " white troops	1868–70	102.62
" " " colored troops	1868–70	42.90
United States Navy	1866	161.93
" " "	1867	113.20
" " "	1868	91.34
" " "	1869	623.18
English Army:		
United Kingdom	1860–62	2.36
Canada	1860–62	16.00
Gibraltar	1860–62	39.60
Bombay	1860–62	121.21
Jamaica, white troops	1860–62	181.81
" black troops	1860–62	70.17
United Kingdom	1867–68	1.77
French Army:		
Home Service	1863–64	18.25
Algeria	1863–64	249.64
Home Service	1866	26.35
Algeria	1866	289.03
Italian Army	1867–69	64.50

The mortality of the civil population of India from "fevers" is given by Fayrer as follows:

Total population, 187,105,833.

Fever deaths, 1877	2,504,493
" " 1878	3,247,371
" " 1879	3,564,035

The remark is made that "in the present state of registration it is not possible to define the special character and type of these fevers. They are certainly, for the most part, malarial in character."[1]

The percentage of sickness and mortality per annum, among the white troops in the armies of the United States, computed from the returns for three years (June 30, 1862, to July 1, 1865), is given in the following table.[2] The figures relate to troops in the field and in garrison; the deaths in general hospitals are not included:

MILITARY DEPARTMENT.	Ratio of cases to mean strength.	Ratio of deaths to mean strength.	Ratio of deaths to cases.
Department of the East	18.63	0.02	0.12
Middle Department	25.20	0.07	0.26
Department of Washington	34.54	0.06	0.18
Army of the Potomac	26.85	0.12	0.46
Department of Virginia	65.12	0.02	0.29
" of North Carolina	108.71	0.36	0.32
" of the South	57.90	0.26	0.46
" of the Gulf	80.34	0.48	0.60
Northern Department	40.56	0.20	0.49
Department of the Ohio	29.41	0.11	0.33
" of the Cumberland	45.49	0.13	0.28
" of the Tennessee	84.81	0.59	0.70
" of the Missouri	49.55	0.25	0.50
" of the Northwest	20.10	0.06	0.30
Pacific Region	19.74	0.03	0.05

NOTE.—For full details with reference to the geographical limits of these various departments, the reader is referred to the volume from which the data have been taken. The following notes are given, however, for the purpose of defining in a general way the limits of the areas to which our figures refer:

The Department of the East embraces all reports received from troops in New England and the Middle States, excepting the State of Delaware.

The Middle Department includes the State of Delaware, the Eastern Shore of Maryland and Virginia, and the counties of Cecil, Harford, Baltimore, and Anne Arundel, in Maryland.

The Department of Virginia includes that part of Virginia south of the Rappahannock and east of the railroad from Fredericksburg to Richmond.

The Department of the South. "Here are included the reports received from the troops at Hilton Head and the various points occupied along the coast of South Carolina, Georgia, and the east coast of Florida."

The reports under the heading Department of the Gulf relate to the troops stationed at the occupied points on the Gulf coast.

The Northern Department includes the States of Michigan, Ohio, Indiana, and Illinois.

Under the designation Department of the Ohio are embraced all reports received from troops in that portion of Kentucky lying east of the Tennessee River.

The Department of the Cumberland "embraces the reports received from the Army of the Ohio, under General Buell, the Army of the Cumberland, under General Rosecrans, and during the first six months the reports from that part of Kentucky lying east of the Tennessee River."

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[1] Op. cit., p. 14.

[2] The data from which the ratios in this table have been computed are contained in the first medical volume of the Medical and Surgical History of the War of the Rebellion.

The Department of the Tennessee was created by General Orders 195, October 16, 1862, to embrace Cairo, Forts Henry and Donelson, Northern Mississippi, and those portions of Kentucky and Tennessee lying west of the Tennessee River.

The Department of the Missouri included the States of Missouri, Arkansas, and Kansas.

The Department of the Northwest includes the States of Iowa and Minnesota and the Territories of Nebraska and Dakota.

The total number of deaths in the United States from malarial fevers during the last census year[1] (1880) was—males, 10,276; females, 9,985; total, 20,261; giving a proportion of 27.61 per 1,000 of all deaths from reported causes, and a proportion of one death to each 2,495 of the population (=0.4 per 1,000).

The total deaths from malarial fevers recorded according to age was:

Under one year	2,002
Under five years	6,182
From five to fifteen	3,482
From fifteen to sixty	7,909

The proportion of deaths from malarial fever to all deaths recorded in the different regions was as follows:

North Atlantic region	4.56 per 1,000
The Lake region	9.74 "
The Gulf coast	65.85 "

Table showing the Total Sickness and Mortality from Malarial Diseases among the White Troops in the Armies of the United States, from June 30, 1862, *to July* 1, 1865, *including Troops in Field, Garrison, and Hospital.*[2]

FEVERS.	Year ending June 30, 1862.		Year ending June 30, 1863.		Year ending June 30, 1864.		Year ending June 30, 1865.	
	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.
Remittent	40,021	370	86,240	1,164	70,718	859	73,386	1,198
Quotidian intermittent	40,330	32	100,144	140	142,846	114	127,393	134
Tertian intermittent	26,766	33	82,460	116	130,411	130	105,834	75
Quartan intermittent	3,526	4	9,872	38	14,175	20	11,132	21
Congestive intermittent	2,233	361	3,959	1,022	3,818	1,029	2,814	727
Total	112,876	800	282,675	2,480	361,968	2,152	320,559	2,155
Mean strength.	288,919		659,955		675,413		645,506	

From this table we obtain the following:

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[1] From the Med. News, Phila., Nov. 25, 1882.

[2] From Table C, page 636, vol. i., M. & S. Hist. of the War.

Year.	Ratio per 1,000 of cases to mean strength.	Ratio per 1,000 of deaths to mean strength.	Ratio per 1,000 of deaths to cases.
1862	390	2.76	7.08
1863	428	3.75	8.88
1864	536	3.18	5.94
1865	498	3.33	6.69
Average...	463	3.25	7.03

Table showing the Total Sickness and Mortality from Malarial Diseases among the Colored Troops in the Armies of the United States, from June 30, 1864, *to July* 1, 1866, *including Troops in Field, Garrison, and Hospital.*[1]

Fevers.	Year ending June 30, 1864.		Year ending June 30, 1865.		Year ending June 30, 1866.	
	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.
Remittent	6,585	296	14,498	421	9,562	285
Quotidian intermittent....	16,239	21	25,796	26	21,957	11
Tertian intermittent......	12,383	19	19,655	23	19,007	12
Quartan intermittent	1,073	6	1,803	7	1,047	2
Congestive intermittent...	1,058	357	929	305	549	132
Total..................	37,338	699	62,681	782	52,122	442
Mean strength.......	45,174		89,193		56,617	

From this table we obtain the following:

Year.	Ratio per 1,000 of cases to mean strength.	Ratio per 1,000 of deaths to mean strength.	Ratio per 1,000 of deaths to cases.
1864	826	15.47	18.72
1865	703	8.89	12.47
1866	920	7.80	8.48
Average...	816	10.72	13.22

A comparison of these figures with those relating to the white troops shows that the ratio of deaths to mean strength was more than three times as great among the colored troops, while the ratio of cases was less than twice as great. As already pointed out (page 89), this is no doubt partly due to increased exposure; but these figures strongly support the view that much of the mortality ascribed to malarial diseases should have been credited to the continued fevers. Thus we find, as would be expected, a larger number per 1,000 of cases of malarial fevers during the third year than during the first year. But instead of a corresponding increase in mortality, which we have a right to expect among troops constantly exposed to malaria, we find that the ratio of deaths to cases is considerably less than one-half as great during the third year as during the first. (See remarks on page 83.)

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[1] From Table CXL., page 710, op. cit.

General Effects of Malarial Poisoning upon the Individual.

Malarial poisoning may be acute from a brief exposure to the poison in concentrated form, or chronic from repeated or continued exposure to malaria in smaller quantity. But the nature of the morbid phenomena induced does not depend alone upon the amount of the toxic agent absorbed, or on the duration of the exposure to its influence. These phenomena also vary in accordance with circumstances relating to the individual, and to external secondary causes. Thus, according to the observations of Colin and others, a primary exposure to malaria in an intense form commonly produces remittent fever. Further exposure, however, does not occasion a second attack of remittent, but gives rise to one or the other forms of intermittent. The influence of heat as a factor in the development of remittent or congestive fevers is also generally recognized; and, on the other hand, refrigeration of the body—chill—is well known as a common immediate cause of the development of a paroxysm of ague in one suffering from malarial poisoning. The paroxysm in this case is evidently of nervous origin, and most modern writers take the view that whether immediately due to the action of the primary cause—malaria—or induced by a secondary cause, these paroxysmal febrile attacks depend upon a disturbance of the nervous centres. The most recent English authority, Sir Joseph Fayrer, says:

> An ague clearly is a neurosis at the outset; the materies morbi, acting on the central nervous system, sets up vaso-motor irritation, which causes dilatation and engorgement of the vessels supplied by the splanchnic, the skin and external parts being brought into an opposite condition. The result is the rigor and pallid, shrunken skin, while there is internal congestion, which is followed by reaction, when the skin and external parts become vascular, the signs of pyrexia appear, followed by profuse sweating, and then a return to the normal condition takes place. Such are the phenomena; but why malaria should produce them we can no more say than why strychnia excites, or conia depresses the cord, or why one set of nerve-fibres determines contraction, another set dilatation of vessels. I doubt if any right explanation of periodicity in disease will be given until we can explain it in health—until we can give the physiological rationale of the cardiac, respiratory, or catamenial rhythm, of the diurnal pulse and temperature wave, and so on. We can only say that certain conditions are induced by poisons or impressions acting on the centres, which in one case modify, in another altogether derange the normal rhythm, substituting for it altered temperature, tissue-change, and exaggerated neuro-dynamic states as seen in the paroxysms of an ague or in the thermic wave of a remittent fever.[1]

The present writer must subscribe to this confession of ignorance as to the *modus operandi* of the malarial poison upon the nervous system; for he is not prepared to accept the explanation of Tommasi-Crudeli, who thinks that the rigors may be produced by the irritation of vaso-motor nerves by bacilli in the circulation, and that the febrile attack is the result of the discharge of the bacilli from their special *nidus* in great quantities.

The view that the primary toxic action of malaria is upon the nervous centres and that the sympathetic ganglia are especially implicated is supported by the symptoms of acute malarial poisoning. These symptoms, of the gravest character, may be developed within a very brief period after exposure. Hertz says: "I have repeatedly satisfied myself that the disease may appear immediately after the reception of the injurious influence. For this purpose I have sat down beside marshy ditches which were in process of drying, selecting those in particular that were distinguished by their putrid exhalations. As soon as within half an hour I would experience a slight disturbance of vision, ringing in the ears, dizziness, a feeling of burning and roughness in the throat, nausea, choking sensations and chilliness, and a few hours later an attack of fever, which was usually light."[1]

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[1] Op. cit., p. 70.

Hertz may have been mistaken in ascribing these symptoms to malarial poisoning, but that effects far more decided, and even fatal, may follow almost immediately after exposure is beyond question. Instances are recorded by MacCulloch and others of persons having died in a few hours in the Maremma of Tuscany (Fayrer); and exposure for a single night in some of the malarious swamps in the southern part of our own country is equally dangerous. The following account of the effects of concentrated malaria is contained in "A Clinical Treatise on the Endemic Fevers of the West Indies," by W. J. Evans, M.R.C.S., London, 1837:

> When the constitution is affected by malaria in a still more powerful manner, the effects are often immediate, and I will describe them as they occurred to myself. I had occasion to visit an estate in the neighborhood of Castries about midnight, and my road obliged me to pass the swamp which lies to the north of the town. There was a lovely moonlight, the sky was unclouded, and a heavy dew was falling. On approaching the swamp I was sensible of an extremely disagreeable odor, arising from its emanations, and from the rank and foul vegetation on its surface and in its neighborhood. I then perceived a peculiarly unpleasant, but indescribable taste in my mouth and pharynx, which produced slight vertigo, nausea, and even efforts to vomit. On my arrival at the estate, which was shortly afterward, I took a glass of hot punch, with the hope that it would allay the nausea; I was, however, mistaken, for it was immediately rejected, and an ague came on, which obliged me to go to bed, where I remained until the afternoon of the following day. After a profuse perspiration I was enabled to ride to town, though still very unwell. At night the symptoms returned with such severity as to require a bleeding from the arm and leeches to the epigastrium; by these means the paroxysm subsided eighteen hours after its commencement, and a return was prevented by the free use of the sulphate of quinine. . . .
>
> About eight o'clock in the evening two boatmen, after finishing their day's work, before returning home were occupied in hauling their canoe high up on the beach, close to the most dangerous part of the swamp mentioned above, when they perceived immediately to windward a small cloud of vapor gradually approaching them, and in a short time they were enveloped in it. One of them fell down, apparently in a state of asphyxia, and the other was so affected as to be unable to render him any assistance. The vapor passed away quickly, and the one who had been the least incommoded recovered sufficiently to look after his companion, whom he found lying in the mud, apparently insensible. He continued in this state only a short time, and gradually became sufficiently well to be led home. In the course of the night Dr. Chevalier was called to see him, and found him suffering from an intense ague. The surface of the body was cold, the countenance expressed great anxiety, the pulse was small and scarcely perceptible, the patient was insensible to surrounding objects, and in a state of coma only interrupted by severe convulsions. The cold stage continued altogether about three hours, and as reaction took place the convulsions subsided; but the coma continued and alternated with delirium. . . . About eighteen hours from the commencement there was remission, or rather a slight mitigation of symptoms, with a partial return of consciousness; it continued only a very short time, and was followed by another paroxysm, equal in violence to the last, except that the cold stage was

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[1] Ziemssen, vol. ii., p. 587.

scarcely perceptible. The patient died about forty hours from the period of exposure. The body was examined while warm; the blood was found fluid, and a small quantity of troubled serum was effused between the arachnoid and pia mater on the surface; the lungs were somewhat engorged, and the stomach intensely inflamed, containing about two or three ounces of blood in its cavity.

The other man never suffered further inconvenience. He said that the vapor had no perceptible smell; that it was warm and moist, like steam, stopped the respiration for a moment, and produced a sense of faintness and trembling of the whole body.

LATENCY OF POISON.—The period which elapses between the date of exposure and the development of a pronounced febrile attack is commonly spoken of as the period of incubation. But in the case of the malarial fevers this period is so variable, and the development of a febrile paroxysm so often depends upon secondary causes, that the term "period of incubation" does not seem applicable, inasmuch as it implies that the poison requires a certain time for development within the body of the infected individual. We therefore prefer the term period of latency, which does not commit us to any theory. But, as already pointed out, it is difficult to reconcile some of the facts relating to this delayed action of the poison with the view that it is not reproduced within the body, and that the effects depend entirely upon the amount absorbed during the time of exposure. As an instance of a comparatively short latent period we give the following example, related by Lind.[1] The Merlin, a small vessel, remained in the river Gambia for six days; during this time a portion of the crew was occupied in cutting wood and another portion in taking on board a supply of water. While in the river all remained in good health, but two days after putting to sea the wood-choppers fell sick, and subsequently those who had replenished the supply of water also succumbed to the malarial poison.

In a very interesting account of the malarial fever known as "Chagres" or "Panama" fever, Dr. Buel,[2] a surgeon in the employ of the Pacific Mail Company, says: "An incubation period of several days, usually not less than a week, elapses between the time of exposure and that of development. On board steamers leaving Panama for San Francisco this is about the period usually occupied in arriving at Acapulco. Cases of fever begin to occur in considerable numbers within two or three days after leaving that port." Fayrer says: "I have known more than one case where a month elapsed after exposure before the first paroxysm of ague ushered in an attack of fever which assumed the remittent form. Simple ague, however, generally occurs earlier, in a few days or even hours."[3] Numerous instances have been recorded of an exceptionally long latent period without any decided evidence of ill-health in the interval.

Dr. Fiedler[4] gives the following examples of supposed long period of incubation. Dresden is said to be usually free from malarious disease, and the same is asserted to be true of Leipzig. But the following cases occurred in these cities which are attributed to exposure elsewhere.

In Leipzig one case had the first attack nine months after exposure to cause; one case six months; one case ten months, and one case eight to nine months. In Dresden one case had the first attack one month after exposure; one case six months, and one case ten months. In the same journal (page 492) is recorded the case of Dr. Kleinstaedler, who went to Nordemey in August, 1861, and from there to Cöln, "where there was no chance of getting intermittent." In May, 1869, eight years after, he was seized with a "colossal severe attack of intermittent."

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[1] Quoted from Colin, op. cit., p. 118, foot-note.

[2] Dr. Wm. P. Buel, Am. J. Med. Sc., Phila., April, 1856.

[3] Op. cit., p. 78.

[4] Arch. d. Heilk., Leipz., 1870, II., p. 245.

In the same journal (December, 1869) Professor Braune gives the following example of supposed prolonged incubation. Twelve persons in the autumn of 1868 resorted to Borkum, an island of East Friedland, for the purpose of taking sea-baths. Two of these suffered attacks of intermittent fever while still on the island. Nine others escaped until the following spring and summer (from six to nine months after exposure), when they also were seized with intermittent. The patients were adults, all of high social position, and most of them females, and belonged to various localities, as Leipzig, Halle, Liegnitz, Atteburg, etc. In these places it is said that intermittent fever did not prevail, *or was present only in a few sporadic cases.* None of the patients had ever before had intermittent fever. "It seemed, therefore, that in all of them the malady must have had its cause in malarious poison received during their autumnal stay in Borkum." Greisinger is inclined to question these extremely long periods of latency, and the present writer would also suggest that evidence of this kind must be received with extreme caution.

Usually the attacks which occur at a distance from malarious localities are in individuals who are victims of chronic malarial poisoning. And not infrequently it happens that characteristic paroxysms of ague are first developed in these individuals after removal from the tropical climate where the exposure occurred, with the effect, perhaps, of producing anæmia, enlarged spleen, etc., which has caused them to seek a restoration to health by change of climate.

In those cases where a brief exposure gives rise to a febrile attack, after a greater or less interval, the patient commonly gives evidence of ill-health some time before the development of the paroxysm. Thus in the account of "Panama fever" by Dr. Buel, above referred to, we read that "the patient experiences for two or three days previous to the attack a general soreness and tenderness in all the muscles and integuments, with loss of appetite and debility." It is well known, also, that manifestations of malarial poisoning, such as malaise, loss of appetite, headache, periodic neuralgia, anæmia, etc., may occur without the development of a characteristic febrile attack. These cases of "masked malarial fever" show their malarial origin by the promptness with which they yield to the administration of quinine and by the tendency to periodicity exhibited by the various morbid phenomena.

EFFECTS UPON THE NERVOUS SYSTEM.—The profound impression exercised by malaria upon the central and ganglionic nervous systems is manifested especially in those cases of acute malarial poisoning in which the symptoms are developed very shortly after exposure to the poison in a concentrated form. This is indicated by the special designations which authors have given to the various types of pernicious fever—congestive, comatose, convulsive, deliriant, algid, syncopal, cardialgic, sudoral, choleraic.

But these intense and fatal manifestations are not due alone to the amount of the toxic agent absorbed. They also depend to some extent on individual peculiarities, and especially upon secondary causes which assist in overwhelming the nervous centres. Among these secondary causes the most potent are an elevated external temperature and alcoholic poisoning. Victims of chronic malarial toxæmia seem to be less subject to these pernicious fevers than strangers who are suddenly introduced into an intensely malarious atmosphere. This is no doubt due, in part, to the more intense action of secondary causes in the case of the unacclimated stranger; but it seems also to depend upon a certain tolerance acquired by the nervous centres to the direct action of the poison.

Such tolerance is not incompatible with the facts relating to increased susceptibility to intermittent fevers as a result of previous attacks. This increased liability to attacks of ague in those subject to chronic malarial toxæmia seems, to a great extent, to be an increased susceptibility to the action of secondary causes, which readily induce a paroxysm in these individuals, while the primary cause does not always do so, even in those who are anæmic and broken down in health as a result of its continued action, so long as they remain in an equable climate.

The supposition that the nervous centres may acquire a tolerance to the direct action of the poison, and that in this way, in a certain sense, a person may become acclimated to malaria, is supported by evidence relating to the non-recurrence of remittent fever. Colin especially insists upon this, and says that those who suffer an attack of remittent are subsequently more liable to ague, but that a second attack of remittent is extremely rare. If this is true we need some such explanation as is above suggested, or we will be forced to the conclusion that the remittent fever, in which one attack protects from future attacks, has a different etiology from the intermittent fever, in which one attack predisposes to future attacks.

The special symptoms which indicate the implication of the nervous system during a febrile paroxysm, such as chill, fever, pain, delirium, coma, etc., will receive attention in the section devoted to malarial diseases. Intermittent neuralgia will also receive consideration in the second part of this volume. But we shall notice here certain exceptional phenomena connected with the nervous system which have been ascribed to the action of malaria.

Various authors have reported cases in which the phenomena of an intermittent paroxysm have been confined to a portion of the body. Thus Dr. W. A. Peck, of Berwick, Pa., gives the case of a young lady in whom the whole right side went through the cold, hot, and sweating stages, all well marked, without any participation of the left.[1]

Griesinger gives several cases of the same kind. "In one patient with complete paralysis of sensation and motion of the lower part of the body, due to fracture of the tenth dorsal vertebra, the paralyzed portions remained unaffected, while the rest of the body underwent a complete paroxysm of fever, with chill, heat, and sweating."

In another patient, after the cure of malarial fever by quinine, regular paroxysms of horripilation and cold continued in an arm which was the seat of a suppurating wound. In a woman sixty-two years old, observed by Griesinger himself, who had suffered for four years from traumatic anæsthesia of the left hand, light attacks of intermittent declared themselves by chilliness and pain in that arm. Hertz, from whom we have quoted, says: "I myself treated a tobacconist in whom malarial fever showed itself by severe, regularly intermitting neuralgia of both lower extremities, with chill and subsequent heat in the same."[2]

Cases of partial paralysis of supposed malarial origin have been reported by various authors.

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[1] Wood's Practice, vol. i., p. 257.

[2] Ziemssen, vol. ii., p. 646.

Macario reports a case of this kind in which a woman was seized, two days after her confinement, without any known cause, with formication in the feet, which then spread to the thighs, the trunk, and the upper extremities, these becoming paralyzed. These manifestations were repeated three times, after the quotidian type, and were arrested by quinine.[1]

This case was not ascribed by the author who reported it to malarial poisoning, and it must be remembered that intermittent nervous phenomena may occur quite independently of this cause. Great caution is therefore necessary in accepting unusual cases of this nature as evidence of the peculiar action of malaria. Nor does it follow that malaria is at the root of a trouble of this kind because a case is benefited by quinine. The favorable action of this remedy in nervous affections is not confined to those of malarial origin. With this caution we report also the following cases:

A woman, sixty-four years of age, after being quite well the day before, was suddenly attacked with paralysis of the lower extremities and sphincters. Sensibility was unchanged, consciousness clear, the temperature normal, pulse eighty, small and empty, no pain in the spinal cord. The next day there was an astonishing change in the condition. The patient can walk again and void urine voluntarily, and only complains of weakness in the legs. The next morning there was paraplegia again, which had set in at the same hour as two days before. A third paroxysm was awaited, which also set in at the appointed time, although without paralysis of sphincters. Quinine effected a rapid cure. (Case reported by Romberg.[2])

The following case is reported by Hartwig:[3]

A vigorous laborer, twenty-three years of age, had suffered from tertian intermittent for a few weeks five years before, but since that time had remained perfectly well and strong. In November of 1873 he first noticed weariness in the legs, which gradually increased, and the arms too were attacked. On the third day he was obliged to take to his bed, and the night following he was completely paralyzed—his legs, trunk, arms, and even the movements of his head were paralyzed, but not the muscles of the face; speaking, breathing, and swallowing were somewhat hindered. There was no paralysis of the sphincters, sensibility was intact, the head entirely free, no pain. The secretion of sweat was excessive. After this condition had lasted for twenty-four hours it let up, and in half an hour, generally with an increased secretion of sweat, all the muscles again became movable.

During the succeeding twenty-four hours the patient remained free from any sign of paralysis, merely complaining of weariness and heaviness of the limbs. Then the attack of paralysis recurred again, in the same way as at first, and then there followed regular successive free intervals and attacks, both of about twenty-four hours' duration. Gradually the time occupied by the attack extended to forty hours, the interval being much shorter. Under the use of arsenic the intervals also extended over a period of about forty hours. On first using quinine the attacks remained altogether absent for four days. After hypodermic injections of strychnia the tertian type of the attacks was re-established. . . . At the end of March, 1874, the following condition was found to exist during the attack: The patient lay then completely paraplegic; only the muscles of the face acted normally; the flexors of the hands and feet showed a minimum amount of motion; the pupils reacted well; the special senses were normal. . . . In the course of the succeeding months greater and lesser irregularities occurred in the course of the disease. The use of quinine sometimes prevented the attacks for a number of days, but then they returned again in spite of its continued use. . . . After the trouble had lasted for seven and a half months no radical improvement could as yet be demonstrated, and nothing is stated with regard to the final termination of the case.

Erb says in regard to these cases: "It is in the highest degree probable that we have here to deal with a malarial infection. The intermittency of the paroxysms, their termination in a sweat, and the efficacy of quinine, all argue in favor of this intermittent paraplegia being nothing else than a masked intermittent. To be sure this cannot as yet be rigidly proven."[1]

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[1] Ziemssen, vol. ii., p. 601. [2] Ibid., vol. xiii., p. 815. [3] Ibid.

The writer would remark with reference to the last case, that if there had been no exposure to malaria since the tertian intermittent from which the patient suffered five years prior to this attack, and from which he perfectly recovered at the time, the supposition that this intermittent paraplegia, which was temporarily benefited but not permanently cured by the administration of quinine, was due to malaria, is very far from being proven.

Other intermittent nervous phenomena which have been observed in the victims of chronic malarial poisoning, and which are directly or indirectly due to malaria, may be mentioned here, such as epileptic or hysterical seizures, periodic vomiting, cardialgia, local hyperæmias, hemorrhages, coryza, bronchial catarrh, etc.

GENERAL EFFECTS UPON THE VISCERA.—Bartlett says, in his admirable treatise on fevers (page 378), that "it can hardly be regarded as hypothetical to say that there is a double element in the pathology of periodic fever. This double element consists in *a perversion of the function of innervation* and of *local congestions in certain organs and tissues.*" At the present day few physiologists would hesitate to include the local congestions under the heading "perversion of the function of innervation." These congestions are commonly, and no doubt properly, ascribed to vaso-motor paralysis. As a result of such vaso-motor paralysis induced by malaria, we may have congestion of the spleen, liver, kidneys, and brain ; and hyperæmia of the mucous membrane of the stomach and intestine. These local congestions give rise to prominent symptoms during the febrile paroxysms induced by malaria, and will receive attention hereafter.

CUTANEOUS MANIFESTATIONS OF MALARIA.—The cutaneous manifestations of malarial poisoning appear also to be of neurotic origin.

Professor Verneuil and Dr. Merklen,[2] who have recently studied this subject, arrive at the following conclusions :

1. Herpes is a frequent manifestation of malaria.
2. It may precede the access of the intermittent fever, or occur during any one of the three stages of the attack or after the sweat. There is consequently no etiological correlation between herpes and the fever, in spite of their frequent coincidence.
3. Malarial herpes possesses no special characteristics. Its most frequent seat of occurrence is on the face, and while usually discrete, it may occasionally become confluent.
4. The black crusts and vesicles of herpes are associated with the graver and pernicious forms of malarial fever.
5. Exceptionally, malarial herpes occurs under the form of zona.
6. In all forms, malarial herpes may be preceded or accompanied by vaso-motor troubles, disturbances of the sensibility of the skin in its neighborhood, and may perhaps indicate a nervous origin of the complication.[3]

GENERAL EFFECTS UPON THE BLOOD.—Next to the nervous phenomena and visceral congestions which characterize periodic febrile attacks induced by malaria, the most notable effect of the poison is upon the histological elements of the blood, and especially upon the red corpuscles, which undergo wholesale destruction during the paroxysms of fever, and also in those cases of chronic malarial toxæmia in which no distinct paroxysms occur.

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[1] Ziemssen, vol. ii., p. 816.
[2] Ann. de dermat. et syph., Par., Nov. 25, 1882.
[3] Med. News, Jan. 13, 1883, p. 39.

This destruction of the red corpuscles is shown by the anæmic appearance of the victims of malarial poisoning, by actual enumeration, and by the presence of dark-colored pigment granules in the blood and tissues which are derived from the coloring matter of the blood. Rokitansky says:

> That the groundwork of pigment is the coloring matter of the blood appears to us proved, the cases in which pigment is obviously derived from hæmatin and blood-corpuscles being so numerous as to exclude all doubts on the subject.[1]

Professor Kelsch, of the military hospital of Val-de-Grâce, has devoted much time to the enumeration of the corpuscles in malarial fevers, and gives the following *résumé* of his observations:

> When the variations in the number of globules in a vigorous man are followed from the first paroxysm to the stage of profound anæmia, it is found—(1) that the anæmia comes on very rapidly. In less than a month the globules fall from five millions to a million and a half or less per cubic millimetre; (2) that there are three stages in the numerical variations of the red corpuscles which correspond with tolerable accuracy to the changes in the fever, as observed clinically. A first and short one, in which the globular deficit, exceedingly rapid, is reckoned by several hundred thousands daily. It corresponds to the initial stage of the fever, when there are acute febrile symptoms of more or less gravity, which are continued or remittent. A second, which lasts longer than the first, during which the deficit for each paroxysm becomes less. The fever is still severe, but the intermitting type has taken the place of the remittent. During these two first stages the globules continue to decrease in number.
>
> Finally, a third, in which the number of globules ceases to fall. It oscillates at first for some time around a minimum. The blood still loses under the influence of the paroxysm, but the losses are less marked than in the two first periods, and are compensated by the salutary influence of periods free from fever, during which the globules are regenerated. This regeneration seldom takes place during the two preceding stages.[2]

The question whether this destruction of the red corpuscles is due to the direct action of the malarial poison, or whether it is secondary and results from the disturbance of innervation and the local congestions which occur during a paroxysm, and to a less extent when no febrile paroxysm is developed, is one of the greatest importance, but one which the present state of knowledge does not enable us to decide.

The observations of Kelsch seem to show that the diminution in the number of corpuscles occurs mainly during the febrile paroxysm. Now we may suppose (*a*) that this is due to the immediate presence, at this time, of malaria in unusual quantity in the blood; or (*b*) that it is due to the local congestions—and especially to splenic engorgement—which occur during the febrile paroxysm; or (*c*) that it is due to elevated temperature and blood stasis combined; or (*d*) that it is due to the presence in the blood of excretory products not eliminated during the temporary paralysis of excretory organs; or (*e*) that a blood poison other than malaria is produced in the body during the febrile paroxysm.

The first hypothesis accords with that which would explain the other phenomena of the paroxysm in the same way, and necessitates a belief in the reproduction of the poison within the body at stated intervals. The fact that anæmia may occur from exposure in a malarial atmosphere independently of the development of febrile paroxysms seems to support this view. But on the other hand, in chronic malarial toxæmia unattended with periodic attacks of fever we have an enlarged spleen—often enormously enlarged in those natives of malarial regions who present a general cachectic appearance and yet seem to enjoy a certain immunity from attacks of ague. It is therefore possible that in these cases also the anæmia is secondary, and results from visceral engorgement due to vaso-motor paralysis.

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[1] Pathological Anatomy, Syd. ed., London, 1854, vol. i., p. 208.

[2] From Edinb. M. J., Dec., 1875. Translation from Arch. de physiol., No. 5, 1875.

Again, we may suppose that the primary action of the poison is upon the blood-corpuscles themselves, and that the nervous phenomena are secondary, being due to the action of products resulting from the disintegration of the corpuscles. It is even possible that the black pigment which is found in the blood during a paroxysm acts mechanically to produce the nervous phenomena. This explanation is no more improbable than that of Tommasi-Crudeli, who imagines that the *Bacillus malariæ* acts in this way, and it has in its favor the fact that these granules are found, upon post-mortem examination, in great abundance in the very ganglia to which we must trace the nervous phenomena of a paroxysm, and where it is not difficult to believe that they may constitute a cause of irritation, especially at the moment of their deposition.

We may have anæmia as a result of many causes other than malarial poisoning. There is doubtless a wholesale destruction of the red corpuscles of the blood in acute febrile diseases generally, and chronic cachectic conditions are attended either with destruction or deficient production of these elements. But it appears to be only in malarial diseases that black pigment is produced as a result of such destruction.

Dr. Forsyth Meigs has given special attention to this point in his valuable researches relating to changes of the blood in malarial fevers.[1] He says:

> In the microscopic study of many viscera and of blood from the portal vein, conducted with special reference to the existence or non-existence of pigment therein, I have failed to find it in cholera, typhus or typhoid fever, the different forms of Bright's disease (acute, fatty, and granular atrophy), jaundice, cirrhosis, cancer and fatty degeneration of the liver, alcoholismus, white cerebral softening, and diseases of the heart. Not having closely scrutinized the tissues with a similar purpose in other of the zymotic or blood diseases than those included in the above enumeration, I can only refer to the many histological researches concerning them familiar to all. But whether pathognomonic or not, the intimate and pre-eminent connection of this pigment matter with the intermittent and remittent affections remains a most interesting fact.

The view that the nervous phenomena in malarial fevers may be due to the deposition of pigment in the substance of the brain and spinal cord, where it is found in abundance upon post-mortem examination, is not a new one. As to its presence Meigs says:

> Beginning at the spleen, which is most constantly and most seriously affected—enlarged, softened, radically changed in color, its tissue and its blood loaded with a new unnatural product—we pass on to the liver. This is nearly always found somewhat enlarged, hyperæmic, of altered hue, and with much pigment entangled in its structure. The blood of the portal and hepatic veins contains often, in very large quantity, pigment granules, grains, cells, and flakes or scales. The capillaries of the cardiac walls have received the same material, and free masses show themselves among the fibres. Again, we find it in the kidneys, caught in the Malpighian tufts, or after rupturing these, in the uriniferous tubules. Lastly, it presents itself in the cerebro-spinal axis, chiefly in the form of minute granules within the capillary tubes, so as to change the natural whitish and gray tints to a leaden or India-ink hue. Nothing I

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[1] Pennsylvania Hospital Reports, vol. i., 1868.

> have seen in pathology has filled me with more surprise and interest than this condition of the nerve centres.[1]

The presence of this pigment in the blood during life has been verified by numerous observers, and recently by Lavaran and Richard, whose studies are valuable as establishing the constant presence of pigment granules and pigmented cells in the blood of malarial fever patients, although we may not be prepared to accept their explanation of the manner in which it is formed—by the parasitic invasion of the red corpuscles.

Dr. Wm. A. Hammond, in a paper contributed to the *St. Louis Clinical Record* in 1877, gives an interesting account of a case in which he verified the presence of pigment in the blood during life. Blood obtained from the finger showed the existence of numerous pigment-holding cells, but no free pigment. The blood of the spleen, withdrawn with a hypodermic syringe, was found to contain numerous pigment-holding cells and masses of free pigment. This latter was generally in granules, sub-rotund in shape, and averaging about $\frac{1}{2800}$ of an inch in diameter. Occasionally these granules were aggregated in groups of irregular form, and again in figures distinctly stellate in shape.

Meigs' observations led him to the following conclusions:

> By a tabulated statement of the one hundred and fifteen observations, and a comparison of these with post-mortem appearances, I feel justified in the following conclusions:
>
> 1. That in examining blood during life with a view to determine the presence or absence of pigment-matter, great care is necessary to exclude all foreign particles from the epiderm and elsewhere.
> 2. That pigment may exist abundantly in the visceral capillaries and in the contents of the portal vein and other large vessels, when blood obtained from the derm and subcutaneous tissue does not exhibit it.
> 3. That only in cases of excessive pigment development will granules and pigment-cells be visible in such blood.
> 4. That in the acute stages of malarial fever the red blood-corpuscles are darker than natural, appear soft, are sometimes crenated, readily yield their coloring material when mingled with water, and are disposed to mass irregularly rather than to form distinct rouleaux.
> 5. That as the disease progresses they are rapidly and very abundantly diminished in number, become pale, lose their tendency to aggregation, and either remain isolated or arrange themselves in imperfect columns.
> 6. That in the early stage of the disease the number of white corpuscles is not perceptibly increased, and that later their increase, though very irregular, is always observable; from six to thirty-five appearing in the same microscope field which presents in normal blood only two or three.
> 7. That excessive anæmia, with a large increase in the number of white corpuscles, may exist in malarial cases without marked enlargement of the spleen.
> 8. That no other morphological alterations are to be detected except, as also in some cases of severe anæmia from other causes, certain colorless, highly refracting granules, free or in membranous-looking fragments, appearing like white corpuscles broken up, and giving to portions of the field a filmy, clouded aspect.[1]

Evidently among the changes noted the only one peculiar to malarial fever is the presence of black pigment, either free or included in "pigment-cells." Meigs says:

> Then again we find these granules contained in cells not otherwise distinguishable from white blood or splenic corpuscles in their ordinary condition. Sometimes these cells have an oblong or spindle-shaped outline. [Body No. 2 of Lavaran ?] They occur most abundantly in the spleen and portal vein, but appear also, in aggravated cases, throughout the organism. In the liver the molecules are seen adherent

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[1] Op. cit., p. 99.

to or contained within the hepatic cells—*i.e.*, within their "formed material." Still other and not less frequent forms are those of the grain and larger mass, which are distributed in an analogous manner, and are found even in the brain in an extra-vascular position. Some of them, upon pressure, look like fragments broken off from yet larger masses. Their size varies indefinitely, from a mere dot up to grains many times as large as red blood-globules. Frerichs states that some of the masses are $\frac{1}{100}$ of a line in breadth and $\frac{1}{70}$ of a line in length; and these he regards as probable casts of the smaller vessels. My own measurements correspond closely with these. I have not recorded any isolated grains of more than $\frac{1}{1200}$ of an inch in breadth, but have frequently observed aggregations of granules and larger masses which measured $\frac{1}{300}$ to $\frac{1}{700}$ of an inch; $\frac{1}{1200}$ to $\frac{1}{1800}$ of an inch was an approximate average size of the separate grains. . . . In shape these pigment-grains are very irregular, rounded or sharp, with an angular, brittle-looking outline. . . . In color the pigment varies almost as much as in size and shape. Usually it is deep black, quite opaque, and with abrupt, non-translucent margins. Then again we find a brown rim through which some light passes. Frequently the color is reddish-brown, or even reddish-yellow, as seen by transmitted light, and the granular scales are seldom opaque. In the splenic pulp I satisfied myself of the existence of red blood-globules in different stages, not only of disintegration, but also of advancing metamorphosis toward black pigment, and am therefore prepared to agree with Frerichs that these different colors represent the various stages in the transformation of the red pigment of the blood into melanotic matter.

The writer has found similar evidence of the transformation of the hæmoglobin of the red corpuscles into granular pigment, varying in color from reddish-yellow to black, in the spleens of septicæmic rabbits, and has consequently objected to this being accepted as evidence of malarial infection in these animals. The fatal septicæmia in the cases referred to was produced by the subcutaneous injection of human saliva, and as the pigment was found in Philadelphia in midwinter, as well as in New Orleans in midsummer, there can be no question of a malarial complication.

The view that the paroxysms of intermittent fever, which may be induced long after exposure by the most trivial secondary causes, may depend in some way upon the presence of this pigment in the substance of the brain and spinal cord or sympathetic ganglia, has much in its favor. Frerichs[1] says with reference to this:

> That these are connected with one another as cause and effect is a probable supposition, which acquires the more weight from the fact that in general there is an unmistakable correspondence between the intensity of the two. Hence the earlier observers, and especially Planer, had no hesitation in attributing the cerebral symptoms to the occlusion of the capillaries with pigment. I cannot give my unconditional support to this view, however plausible it may at first sight appear, because a close analysis of the observations and a careful comparison of the anatomical lesions with the symptoms during life render the connection between the two as cause and effect, in many cases at least, doubtful.

We think with Frerichs that this mechanical explanation of Planer is not a satisfactory explanation of the nervous symptoms—headache, delirium, coma—which characterize a paroxysm of congestive intermittent, for example. The sudden transition in these cases, under the influence of full doses of quinine, from the most alarming condition to one in which the mind is clear and the patient in every way comfortable and apparently restored to health, is hardly consistent with the view that the coma and other nervous phenomena are due to occlusion of the capillaries with pigment. But that extra-vascular pigment may be the exciting cause of such a paroxysm—the match which starts the conflagration—is a more plausible hypothesis. Meigs discusses this hypothesis in so able a manner that we feel no hesitation in quoting still further from his valuable paper.

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[1] A Clinical Treatise on Diseases of the Liver. Murchison's translation, London, 1860.

> How long does the pigment-matter remain fixed in the organic structures ? No precise answer can as yet be given to this question, but such facts as have been recorded tend to confirm the idea presented above, that the period must be a long one. . . .
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> The great importance of this fact becomes manifest when we pass on to inquire in what degree this product of diseased action is itself a morbific agent—*i.e.*, how far it may derange the action or impair the function of those organs in which it lingers. In attempting to determine the significance of any particular element as a factor in the production of the phenomena of disease, we are at once perplexed by the uniform obscurity with which, beyond a certain point, the etiology of constitutional disorders is enveloped. Not understanding the essential character of the original poison, nor its immediate mode of operation, we cannot know how many of these phenomena are to be referred to the *direct* action of this poison upon the chemical constitution of the blood and tissues or to its specific influence upon the various organs ; and how many, on the other hand, must be included among its *indirect* or secondary results consequent upon such primary alterations. Thus the stupor and delirium of typhus may be plausibly referred to a direct impression upon the cerebral centres, or intrepreted as an "oppression" of those centres by the products of destructive metamorphosis which load the blood. But however classified, these various conditions cease permanently when the patient becomes convalescent, and the original poison, together with its products, disappears from the system. Not so in malarial affections. Their history presents a peculiarity which is in strong contrast with what is known concerning all other "blood diseases." I do not now refer to that persistent cachexia into which a protracted intermittent or remittent fever too frequently passes ; for although its features are so singular as to lead us to suppose, *à priori*, that some deleterious matter must be retained within the body, yet to a certain extent they find their analogues in the mental and physical debility and organic lesions which succeed severe attacks of typhoid fever, scarlatina, diphtheria, and their companion disorders. The distinguishing character of miasmatic fever is its tendency, during one, two, or many years after the patient has apparently recovered, to recur without any fresh exposure to the cause. Other constitutional affections either leave no such tendency behind them or positively protect the individual against a repetition of their visit.
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> When, therefore, on the one hand, we fail to find any abnormal substance within the organism in cases where this tendency does not exist, and on the other uniformly discover an unnatural matter diffused through the organs in the only disease where such a tendency is present, the mental process which suggests that the two facts are intimately connected becomes something more than pure speculation. This tendency varies very much in individual instances ; so also does the amount of pigment produced. How far the strength of the one corresponds to the amount of the other we must leave to further observation to determine. I only offer the suggestion. It would be easy to frame hypotheses as to the manner in which the existence of pigment might promote the return of the malarial paroxysms. Thus the masses might be supposed to retain in a dormant state the original poison from the union of which with the blood-corpuscles they had resulted. Then if the circumstances—such as overexertion in hot weather—which are prone to bring on a renewal of the disorder are those also which facilitate the resorption of this matter into the blood, the miasmatic influence would be again set at liberty to act.[1]

Another hypothesis, which is perhaps more plausible, is that pigmented nervous centres are peculiarly irritable, and that when from exposure of the surface of the body to chill, or from any other cause, they become temporarily hyperæmic, this irritability gives rise to the disturbance of nervous equilibrium—the nervous explosion, so to speak, which constitutes the phenomena of an attack of ague.

Meigs mentions the fact that in anæmia resulting from malarial poisoning the red corpuscles become pale, but he does not refer to the change in the dimensions of these elements which has been noted by several observers.

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[1] Op. cit., p. 102.

Hayem[1] has shown that this is a change which occurs in anæmia from any cause, and that it is not more marked in malarial toxæmia than in other chronic cachectic conditions. According to this author, whose extended researches enable him to speak with authority upon this subject, the red corpuscles in anæmia differ from those in normal blood in their color and dimensions. The decoloration may easily be detected by an experienced eye upon microscopic examination of blood diluted with a suitable liquid, or of a dry preparation of corpuscles spread upon a thin glass cover. The loss of color will be more easily recognized if a specimen of normal blood is examined at the same time.

The morphological changes depend upon the presence of a considerable number of corpuscles, which vary in a notable manner as regards size, some being smaller and some larger than the standard corpuscles of healthy blood. Hayem says that the most frequent modification results from the accumulation of elements below the size of the normal blood-globules, and that these are sometimes extremely small. These he calls "dwarf globules." They are believed by this author to be young, incompletely developed red corpuscles. With reference to them Hayem says:

> They are to be found in anæmia from any cause, without exception; as well in the symptomatic anæmias as in those which are called spontaneous. They do not in any way characterize the grave anæmia called pernicious, as has been recently claimed by Eichhorst. On the contrary, the small globules are especially abundant in anæmia of moderate intensity.
>
> With reference to the facility with which they are transformed into spherical globules, a property which has caused them to receive the name of microcytes, I have expressed the opinion that they are not found in the blood in circulation in this spherical condition. All of these *hématies*, from the time that they can be recognized as distinct elements, are discoid and biconcave. The transformation into microcytes is the consequence of the action of exterior agents. The young globules are more vulnerable than the completely developed adult globules, and this fact may be observed not only in the blood of anæmia, but also in a physiological condition, in the new-born for example, whose blood always contains a small proportion of these dwarf globules.
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> Beside the dwarf globules we place naturally the monstrosity in the opposite direction, the voluminous, or giant globule. Its physiological signification is less clear, but this hypertrophy is also a fœtal form, a sort of return toward the embryonic state.[2]

The writer is able to verify these statements relating to the morphology of the corpuscles in the anæmia resulting from malarial fevers, and has in his possession a series of photo-micrographs made in New Orleans in 1880 from the blood of selected cases of malarial toxæmia in the Charity Hospital, which show the over- and under-sized corpuscles in a most satisfactory manner.

Effects upon Wounds.—Sir Joseph Fayrer, in his Croonian lectures, quotes the remarks of Mr. Eccles, a surgeon of the Stafford House Ambulances during the late Russo-Turkish campaign, with reference to the local effects of malarial poisoning upon wounds, and states that he is able to confirm from experience the observations of Mr. Eccles, which are summarized as follows:

> The local effects of malarial fever on wounds differ according to the stages. In the cold stage the discharge decreases in quantity, and sometimes, if it be prolonged, ceases altogether; the surfaces of the wounds will look bloodless or appear congested, and change in color from a bright red to a dull purple or gray hue, the granulations being

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[1] Recherches sur l'anatomie normal et pathologique du Sang. Paris, 1878.

[2] Op. cit., p. 93.

pale and bloodless. Pain is rarely complained of, a sense of numbness being often referred to the wound. In the hot stage all the local symptoms undergo a decided change—the discharge becomes thick, copious, and sometimes fetid. Sloughing occurs in many cases; the surface of the wound looks angry and inflamed; the granulations are florid, sensitive, and bleed on being touched; sometimes on removal of the dressings the surface of the wound is bathed with blood, the edges are puffy, swollen, glistening and painful, an area of redness extending some distance round the wound, with burning or throbbing in the seat of injury. During the intermission the wound generally resumes its ordinary appearance, but not unfrequently the inflammatory action set up during the hot stage continues, and the local effects remain after the cause has ceased to exist.[1]

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[1] Report of the Stafford House Committee, p. 152.

CHAPTER V.

ANTIDOTES TO MALARIAL POISONING.

We are unable to place at the head of this article *Antidotes to Malaria*, for the reason that we are by no means convinced that the remedies which cure malarial fevers do so by neutralizing the malarial poison. Two explanations are possible: (*a*) The toxic agent may be neutralized by the remedy which arrests an intermittent or remittent fever; (*b*) the effects of this toxic agent upon the system may be neutralized. We have seen that the effects of the malarial poison are manifested most prominently upon the nervous system and upon the red corpuscles of the blood. But we have not been able to determine definitely whether the nervous phenomena and the destruction of the red blood-corpuscles are both due to the primary and direct action of the poison, or whether one of these effects is secondary and possibly dependent upon the other.

In the present article we shall consider, in a general way, the action of the remedies which have been demonstrated to have the power of arresting the progress of malarial diseases, with a view to ascertain what light, if any, the facts relating to this antidotal action throw upon fundamental questions concerning the nature and *modus operandi* of malaria.

Quinine.—We shall not at present consider the comparative value of the cinchona alkaloids in malarial fevers, but selecting that one which is everywhere recognized as the remedy *par excellence* in these diseases, will review briefly the facts relating to its physiological and antidotal action. That quinine in full doses is a potent nervous sedative is well established, but authors differ with reference to its primary action in small doses, which according to some is that of a stimulant to the nervous and circulatory systems. Manson believes that the transient perturbation of the nervous system and circulation observed soon after the ingestion of sulphate of quinine in small and repeated doses is probably due to its local action upon the stomach.[1]

According to Binz, the effects of large doses (over fifteen grammes), or of small doses frequently repeated at short intervals, are as follows: 1, Disturbance of the nervous system and of the heart's action, producing general prostration and feebleness of the cardiac movements; 2, chronic disturbance of the brain; 3, disturbance of the organs of speech, occasionally entire loss of speech, for a longer or shorter period; 4, more or less complete, or even incurable amaurosis of one or both eyes; 5, hemorrhage from the lungs (probably) and eruptions on the skin; 6, irritation of the intestinal canal from the arrest of the ordinary movements by the action of the quinia; 7, catarrhal inflammation of the urinary bladder.[2]

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[1] Otis F. Manson, M.D.: The Physiological and Therapeutic Action of the Sulphate of Quinine. Virginia Med. Month., Richmond, Jan., 1882, p. 383.

[2] Centralbl. f. d. Med. Wissensch., Berl., 1872.

The toxic effects of a large dose are shown by the following record of a case which occurred in the practice of Dr. Giacometti, of Mantua, Italy:

> A man from forty-five to fifty years of age having taken at a single dose about two hundred grains of the sulphate of quinine by mistake for cream of tartar, was first seized with cardialgia, nausea, faintness, and entire inability to move. When seen by Dr. Giacometti, eight hours after having taken the dose, he was found in the following condition: The temperature of the body was below the normal standard, his extremities cold, his lips and fingers livid, and his breath fetid. His respiration was slow and gasping; the pulse regular, but so feeble as to be hardly perceptible; his voice inaudible; the pupil extremely dilated, and his hearing and sight almost extinct. His tongue was not dry, but pale and covered with thick and viscid mucus, and the patient was thirsty. . . . On the fifth day the patient could sit up for half an hour, but he could not stand on his feet, so great was his prostration. The feebleness of hearing and seeing, although diminishing every day, did not cease completely for a long time.[1]

According to Dr. George B. Wood, the sedative effects of large doses of quinine are probably indirect, and depend upon congestion resulting from over-stimulation and upon secondary exhaustion of the nervous centres. In support of this view he says:

> The flushed face, the feeling of tension or fulness in the head, the sensitiveness to light, the buzzing and roaring in the ears, the vertiginous sensations, the involuntary muscular movements, the increased frequency of pulse and heat of skin, and the active delirium and convulsions which occasionally though rarely occur, are all proofs of stimulation and active congestion of the brain; and these proofs are still further strengthened by the fulness of the vessels of the pia mater, universally observed on post-mortem examination, and the evidences of positive meningitis, which have been observed in a few instances.[2]

More recent authorities agree that the effect of full doses of quinine is to diminish the frequency of the pulse and to lower the temperature; and the sphygmographic tracings obtained by Dr. Mary Putnam-Jacobi, in a case in which the brain was exposed by an opening in the cranium, show that a full dose (20 gr.) caused "diminished energy of the cardiac contractions, unfilled cerebral arteries, and great diminution in intercranial pressure." In the same case a dose of five grains of quinia was found to increase the energy of the cardiac systole and the tonus and elasticity of the cerebral vessels, "so that the blood is forced rapidly on through the capillaries, thus diminishing the resistance to the cardiac systole. More blood is admitted to the brain, but the intercranial pressure is lessened."

M. Sée has arrived at the following conclusions: "In health quinine has a three-fold action: first, it diminishes the frequency and force of the action of the heart; secondly, it lowers the tension in the arterial system; and, thirdly, it lowers the temperature, or prevents its elevation by exercise, etc."

Experiments upon animals show that in poisonous doses quinia may promptly arrest the action of the heart, especially when injected into the veins.

According to M. Briquet,[3] the sedative action of quinia is more decided upon the heart than upon the brain. His experiments led him to the following conclusions:

> 1. That the sulphate of quinine, acting directly upon the encephalon, presents in this action a first period, in which is exhibited clearly an excitement of that organ, but that this period is of brief duration and the effects of *moderate* degree.

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[1] Dict. de méd., xxvi., 568, quoted from Manson.

[2] Therapeutics and Pharmacology, vol. i., p. 242.

[3] Traité Thérapeutique du Quinquina.

2. That in the second period, which occurs promptly and endures for a long time, signs of sedation are manifested, which from their degree and importance constitute, in a manner, the veritable action of the agent.

3. That the brain resists the sedative action of the salt with more energy than the heart.

4. That in cases where the introduction of the sulphate of quinine is effected slowly and gradually, no phenomena of excitation are observed; the animals only present titubation, debility, torpor, and disinclination for exertion; that the steps are slow, uncertain and vacillating; their feet separated far apart to enlarge the base of sustenation; they appear stupefied, and their pupils are greatly dilated.

5. That this action of quinine is purely dynamic, and only attains to the degree of inflammation in rare cases where its action has been too energetic or too direct.

6. When the injections of quinine are made into the femoral artery, the pleura, and the cellular tissue, the same series of symptoms were always seen *except those of the period of excitation, the period of sedation only having been present.*[1]

The action of quinine upon the nervous system is further shown in certain cases by the production of permanent or temporary amaurosis, of deafness, and of cutaneous eruptions evidently of nervous origin.

According to Knapp, the characteristic features of quinine amaurosis are: "1. Total blindness after taking a large quantiy of quinine. 2. Pallor of the optic disks. 3. Marked diminution of the retinal blood-vessels, in number as well as in size. 4. Contraction of the field of vision. The *total* blindness is only temporary. Relapses appear to occur, and from comparatively insignificant doses."

The effect of doses of from ten to fifteen grains of quinine upon the visible parts of the auditory apparatus is, according to Roosa, as follows:

The outcome of a series of experiments upon animals by Dr. William A. Hammond, and upon the living subject by the author cited, showed that in these doses the remedy "appeared to cause vascular injection of the auricle, auditory canal, and drum-head."[2]

In certain rare cases a small dose—three or four grains—of quinine produces, within a brief time, an eruption of urticaria, or a bright erythematous blush over the whole surface of the body, attended with intense burning and itching, with congestion of the conjunctivæ and nasal mucous membrane, and with more or less œdema of the face and limbs. A case of this kind has come under the writer's personal observation, and as it occurred in his own family he has been able to demonstrate that the idiosyncrasy is of a permanent character, as attempts to administer the medicine on several occasions, at intervals of a year or more, have invariably been attended with the same results.

The influence of quinine upon the stomach is stimulating in small doses and irritating in large and repeated doses, especially when there is any inflammation of the mucous membrane.

Cohnheim, Binz, and others have shown that quinia exercises a restraining influence upon the amœboid movements of the white blood-corpuscles.

Binz has also proved by experiment that one part in 20,000 dissolved in water will, in a few moments, cause paramecia to show signs of feebleness; that after a longer time their movements are entirely arrested, and that in two hours their vitality is destroyed and they undergo disintegration.

The schizomycetes are less susceptible than the parameciæ to the action of quinia, but the experiments of Ceri and others show that these low vegetable organisms are also restrained in their movements and reproductive activity by quantities varying from 1 to 800 to 1 to 10,000.

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[1] Quoted from Manson, op. cit., p. 351.

[2] The Medical Record, New York, Feb. 10, 1883.

All of these facts go to show that quinia paralyzes and finally extinguishes the vital activity of living protoplasm, animal or vegetable; and it seems probable that the impression made upon the nervous centres of man and of the higher animals by full doses of the drug is the same in kind as that which restrains the activity of paramecium or of the white blood-corpuscles.

It is probable, also, that the protoplasm of gland-cells—liver, spleen—is acted upon in a similar manner, although perhaps to a less degree than in the case of nerve-cells.

Ranke and Kerner have found that in large doses quinia diminishes tissue changes, as is shown by the smaller quantities of urea and of uric acid excreted. This may be due mainly to its sedative action upon the protoplasm of nerve-cells, by which the functional activity of the heart and other organs is restrained; but it is probably partly due to the direct sedative action of the drug upon the protaplasm of the cellular elements of the tissues generally.

The fact that when quinia cures intermittent fever it also contracts the spleen, if that organ is enlarged, is a familiar one. It is also known that when quinia is largely administered to animals for various experimental purposes, the spleen is found pale and hard and its capsule wrinkled. These effects occur even when all the nervous trunks supplying the organ are divided. Hence it is concluded that quinia must act upon the internal nervous system of the spleen (Binz). The function of the organ, it is added, being to form the white corpuscles of the blood and to prepare various oxidized substances, and especially uric acid, for excretion, and quinia having the power of restraining both of these operations, necessarily the organ appropriated to them must contract in proportion to the restriction of its functions.[1]

Quinine is mainly excreted with the urine, but Bochfontaine[2] has recently ascertained that when administered hypodermically it may be found in vomited matters, showing that it may also be eliminated by the stomach.

The facts relating to the therapeutic and prophylactic action of quinine in malarial diseases will now be briefly reviewed, for the purpose of ascertaining what light they throw upon the *modus operandi* of the remedy.

We may say, in general, that moderate doses of quinine prevent the development of the symptoms of malarial poisoning in those who have been exposed to the action of malaria; that the administration of doses sufficient to produce the physiological effects of the drug commonly interrupts the series of paroxysms induced by malaria—intermittent fever; and that the most threatening manifestations of intense malarial toxæmia are very often promptly relieved by heroic doses of the remedy.

The question, then, is whether this remedy is an antidote to malaria or a physiological antidote to the effects of malaria upon the individual?

The latter view is probably the correct one, and, as we shall presently see, it has the support of many of the highest clinical authorities of the present day. But it is possible that this expresses only a part of the truth, and that quinia also prevents the development of malaria in the body by its power to destroy or prevent the development of malarial germs. This would make it an antidote to malaria if these germs are directly the cause of the phenomena of malarial poisoning. But this supposition is opposed by so many clinical facts, and is so far from being established by microscopical researches, that we cannot give it further consideration at present.

We are not, however, inclined to reject the view, elsewhere suggested in this volume (page 77), that the micro-organism which produces malaria in favorable locations external to the body may also produce it within the body, and that in this case its habitat is the alimentary canal (or the spleen, as claimed by Tommasi-Crudeli), where it may be destroyed by a germicide agent, while the effects of the poison—malaria—evolved during its vital activity can only be neutralized by a physiological antidote.

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[1] The National Dispensatory, Philadelphia, 1879, p. 1173.

[2] Revue Scientifique, Feb. 24, 1883.

The fact that larger doses of quinine are required to produce the physiological effects of the drug in an individual suffering from malarial toxæmia than in one in perfect health cannot be accepted as evidence that malaria is destroyed or neutralized in the system by this agent, any more than the tolerance to opium in belladonna poisoning, or the reverse, is evidence that these poisons neutralize each other in a chemical way. The tolerance to the action of quinia which seems to be acquired by those who have been dosed with it for a long time, and its failure to cure intermittent fevers in certain cases, is opposed to the view that this agent is a chemical antidote to malaria. Moreover, the fact that it cures intermittent fevers not malarial, and is recognized as a most valuable remedy in thermic fever, compels the admission that its value as a therapeutic agent depends, to some extent at least, upon its physiological action.

The prompt benefit resulting from the use of *large* doses of sulphate of quinine in the more severe forms of malarial fever has been described in a graphic manner by many of the most experienced practitioners in malarial regions.

Thus we have the evidence of Maillot[1] that the pernicious malarial fevers of Algeria, characterized by all the symptoms of ardent fever—an atrocious headache, delirium, convulsions, coma, a hard, full, and frequent pulse, dry, burning skin, inextinguishable thirst, dry tongue, etc.—were promptly cured by doses of twenty to eighty grains of quinine, these phenomena disappearing "as by enchantment" (Manson).

Surgeon Charles McCormick, United States Army, says:

> Given in large doses boldly and freely during the high febrile excitement of idiopathic and arthritic fevers, it [sulphate of quinine] will be found to lessen the force of the pulse, diminish the heat and dryness of the skin, relieve restlessness, and throw out on the surface a general warm and free perspiration; in short, in a few hours—generally from three to four—it will cut short the paroxysms and arrest the further progress of the fever.[2]

In his work upon the "Diseases of the Interior Valley of North America," Dr. Drake gives evidence to the same effect. He says:

> When its operation in *liberal doses* is noticed it will be observed to diminish the frequency and spasmodic force of the heart's contractions; expand and soften the pulse; increase the functions of the skin, and tranquillize the innervation. . . .
>
> I recently gave a negro boy under twelve years of age about fifty grains of quinine within twelve hours, without producing deafness or ringing in the ears. Its good effects, however, were none the less evident.[3]

Professor Sée, in a series of clinical lectures upon the therapeutic value of quinine, concludes that the drug cannot be considered a specific or counter-poison—

> Because (1) it does not prevent malarial poisoning when taken as a prophylactic; (2) it does not prevent recurrence after a variable period; and (3) it is useless in some

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[1] Traité des Fièvres Intermittentes. Paris, 1866.

[2] N. Orl. M. & S. J., vol. ii., p. 290.

[3] Quoted from Manson.

of the most fatal forms, especially where the fever tends to assume a continued type. Moreover, he points out that in other fevers which present the characters of periodicity and the occurrence of initial rigor—*e.g.*, urethral fever from catheterism—quinia has an equally beneficial effect. He believes that the effect of quinia in ague is due to its threefold action, exerted chiefly during the period of rigor: by its action on the heart it diminishes its frequency and force; on the peripheral arteries, it lowers their tension and produces dilatation; on the spinal cord and vaso-motor centres, acting as a sedative, it tends to diminish their excitability; and, lastly, it exerts a direct cooling action on the system generally; the latter, however, being the least important factor.[1]

Colin, after giving an account of the experiments of Pringle, Polli, and Binz, relating to the antiseptic power of quinine, remarks as follows:

> Finally, nothing yet indicates to us in a positive manner the precise action of the sulphate of quinine; we have no proof of its direct influence, in the organism, upon the morbid principle of the malady. On the contrary, the frequency of relapse in individuals who have taken considerable doses of this medicine, and who have not subsequently been exposed to infection, would seem to prove that the sulphate of quinine does not cure intermittent fevers by its action upon an injurious material imprisoned in the organism, and that its virtue is only exercised against the actual manifestations of poisoning—in a word, that it is simply a remedy for the symptoms.[2]

Finally, we quote the eloquent language and able argument of Trousseau in support of the view that the beneficial action of quinine is independent of any antidotal action against the malarial poison:

> Cinchona, that wonderful remedy about which, for two centuries past, so much has been written, and too much cannot be written, has several modes of action, according to the doses in which it is given.
>
> But independently of this, it seems beyond a doubt that among its precious properties there are two which chiefly distinguish it. The first and most heroic is that which it exercises upon diseases produced by miasmatic infection, under whatever form and type they may appear. The second is that of modifying or suspending the intermittent type of diseases, whatever may be their determining cause, and especially when this intermittent type is at the same time periodic and regular.
>
> In the observations of these two very distinct sorts of effects there is a touchstone very fit to resolve the difficulty which we have just brought up against the nosographists.
>
> In fact, if cinchona, given in the periodic intermittent affections which have no relation of nature and cause to those which originate in the miasmatic affection, suspends or modifies the periodic affection without curing the disease of which this type is symptomatic, it is necessary to conclude that it enjoys (as has been very well said) a general periodic virtue. And if, on the other hand, when given in the periodic intermittent fevers produced by the special marsh poison, it not only suspends the febrile attacks but at the same time destroys the disease of which they are symptomatic, it seems to us that we ought to draw the other inference, that in the latter cases it manifests something besides an antiperiodic action, namely, a virtue remarkably contrary to the special diathesis contracted by the organism under the influence of marshy emanations. This last conclusion would be rigorously legitimate if observation showed that cinchona cures miasmatic fevers, not only when intermittent but also when continued, and it would be still more so if facts proved that the paludal cachexia and the material lesions which it causes yield to cinchona like the intermittent fever itself, of which they are too often the fatal termination.
>
> Here are certainly two very different kinds of action if we consider the result, but if we interrogate the cause we shall perhaps find that they do not necessarily presuppose a distinction in its fundamental action. Whether intermittent, remittent, or continuous, paludal affections do not differ essentially. The type has its causes in the laws of life, and the latter presents all the periodic modes in the regular fulfilment of our functions.
>
> On what, then, can this remarkable difference in the action of cinchona depend, which now takes away the form and basis, and now suppresses only periodic manifestations of symptoms, leaving in its living entirety the inner tendency to reproduce

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[1] Lancet, London, Aug. 8, 1874.

[2] Op. cit., p. 380.

> them? It springs from two causes, the one real, the other only apparent. It is real and positive that in a great number of cases where the paludal affection is neither old nor profound, and which manifest themselves in the form of legitimate intermittent fevers, cinchona, given methodically, often takes away the basis of the disease with its form, the inner principle of the attack with the attack itself. But what follows? That cinchona has destroyed the paludal miasm immediately in the manner of a counter-poison? Nothing proves this, and all seems to unite to prove the contrary.
>
> The paludal impregnation of the system is exterior. With whatever facility the pathological assimilation of the miasm may occur through the morbid properties of the system, and however little analogy there may be with poisons properly so called, this agent is not a morbid poison; or at least it does not seem to be one of the morbid poisons of man, for it never develops itself in us in the absence of the external conditions in which it ordinarily originates. It ought to be, consequently, less adherent to the constitution than the diseases such as gout, syphilis, dartre, etc., which spring spontaneously from our depths as products of that which is originally morbid in us. It follows that if the paludal affections are recent, slightly identified with the system, intermittent, and particularly if regularly periodic (a sign of slight infection which has not produced cachexia), cinchona, in suppressing the periodic symptoms—that is, in fortifying the vital resistance against the return of the febrile access—will give to the system the force and the time necessary to overcome the deleterious power of the miasmatic principle. Everybody knows that many simple intermittents recover by themselves without the aid of cinchona. And how often do we see intermittent fevers, even apparently the least ancient and the least profound, suppressed at first by the bark, then relapsing with discouraging obstinacy in spring or autumn under the influence of taking cold, of an emotion, of an intercurrent malady, and thus throwing discredit on the professed specific virtue of the febrifuge! In fact, nothing happens here except what happens in the periodic symptoms of gout, rheumatic or other sorts; and if the latter yield less readily and relapse under the same form or another type with much more tenacity, it is because the gouty diathesis, for example, is wholly personal and inseparable in a way from the constitutions wherein it is developed, while the paludal affections are accidental and essentially curable. To this we reduce that occult virtue, that celebrated specificity of cinchona in intermittent fevers: *It is no more a direct antidote of the paludal principle than of the gouty principle.*[1]

If we agree with Trousseau in this conclusion, the question still remains whether quinia may not be an *indirect* opponent—we cannot say antidote—to malaria, by preventing its production in the system?

If this toxic agent is reproduced in the system, there is good reason for believing that micro-organisms of some sort are concerned in this reproduction. The facts, therefore, relating to the action of quinia upon low organisms—schizomycetes—are extremely interesting and important in the present stage of the inquiry. The latest and most elaborate experimental research in this direction is that of Professor Ceri,[2] of Camerino, Italy.

In these experiments culture solutions containing quinine in various proportions were infected with a drop of turbid fluid of malarial soil—earth shaken up with water. In a series of experiments in which the quantity of quinine varied from 1 to 100 to 1 to 100,000, it was found that no development occurred when the proportion was below 1 to 900. Non-putrid development commenced between 1 to 1,000 and 1 to 1,500.

In another series of eighteen experiments in which the culture liquids were infected with a gelatine culture of malarial soil, development did not occur in the solution containing 1 to 1,500; non-putrid development occurred in the solutions of 1 to 2,000 up to 1 to 3,000; and the development was accompanied by putrefaction in the solutions containing 1 to 9,000 and less. Many other experiments were made, and Professor Ceri arrives at the conclusion that "the muriate of quinine, in the proportion of 1 to 800, prevents the development of any infectious germs, but that the fertility of a culture may depend upon the quantity of the infectious material. By the aid of a second thorough infection, cultures which after the first had been sterile for a long time may be made fertile."[1]

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[1] Trousseau and Pidoux: Treatise on Therapeutics, American ed., New York, 1880, vol. iii., pp. 157–9.

[2] Dr. Antonio Ceri: Arch. f. Exper. Pathol. und Pharmacol., Bd. 15, Heft 324, and Bd. 16, Heft 122, 1882.

ARSENIC.—The second place as a remedy for malarial diseases must be accorded to arsenic, and we have to inquire, as a check upon any deductions which may be made from the physiological action of quinia, whether the beneficial action of this drug can also be accounted for upon the supposition that it is a physiological antidote to the effects of the toxic agent rather than a chemical antidote to the poison itself, or a germicide solely.

We have ample clinical and experimental evidence that arsenic has a powerful influence upon the nervous centres, and especially upon the sympathetic ganglia; whereas the germicide power of the preparation usually prescribed—Fowler's solution—is very slight.

As examples of diseases of neurotic origin other than intermittent fevers which are favorably influenced by the administration of arsenic, we may mention spasmodic asthma, chorea, angina pectoris, and neuralgia.

The effects upon the nervous system of poisonous doses of arsenic are stated as follows by Philipps:[2]

> The effects of poisonous doses (6 to 8 grs) are often ushered in with rigor, profound depression, and extreme anxiety. Restless tossing of the arms is commonly noted, and later, numbness, cramps, and twitching of the muscles. The œsophageal spasms may simulate those of hydrophobia, and the muscular cramps may amount to opisthotonos; convulsions alternate with delirium, the special senses become impaired or lost, the mental faculties torpid (the stupor may suggest narcotic poisoning), and syncope or collapse may close the scene. There may be local palsies, as of limbs and sphincters. . . . Arsenic exerts a paralyzing influence certainly upon sensory and motor, and we may say *probably* upon vaso-motor nerves also. . . . Poisonous doses markedly depress the circulation, and ultimately arrest heart action (in diastole) in the lower animals. . . . We may note that if death occurs [in man] in a few hours, it is generally from *cardiac palsy*, and is preceded by excessive prostration and fainting.

As in the case of other agents which act powerfully upon the nervous system—*e.g.*, opium, tobacco—(malaria?) a tolerance to the effects of arsenic may be obtained by using it habitually in gradually increasing doses.

Arsenious acid is known to be a potent antiseptic agent, but according to Koch a one per cent. solution is required to destroy the germs of bacilli, the time of exposure being ten days. If, therefore, the object of medication in malarial diseases is to destroy the spores of *Bacillus malariæ* stored away in the spleen or elsewhere, it is evident that five-drop doses of Fowler's solution, administered twice daily, would be quite impotent. Yet these doses may arrest the course of an intermittent fever, and there is good evidence that still smaller quantities have a prophylactic value. But the writer's experiments indicate that the germicide power of Fowler's solution cannot be compared with that of arsenious acid, and that so far as the test-organism employed is concerned it is practically *nil*. Thus in six experiments in which the micrococcus of pus was exposed for two hours to the action of this agent in the proportion of 4, 8, 10, 20, 30, and 40 per cent., the vitality of the micrococcus was preserved in every case, as was demonstrated by its subsequent abundant multiplication in a sterilized culture solution. It is very possible, however, that other micro-organisms may have less resisting power.

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[1] Quoted from the Medical Times, Philadelphia, Dec. 16, 1882.

[2] Materia Medica and Therapeutics, Am. ed., New York, 1882, vol. ii., p. 31.

CARBOLIC ACID.—The reports as to the value of this agent in the cure of intermittent fever are quite contradictory. Thus Curschmann,[1] of Berlin, as the result of numerous trials, reports it worthless, as does Surgeon McNally,[2] of the Indian Medical Service. Other reports, however, have been more favorable. Surgeon Worgan, of the Third Indian Regiment, says that to be effectual the doses must be full and frequent; ten minims of pure acid to the ounce of water, one and a half ounce of the mixture being given six times a day. If we admit that carbolic acid in these doses cures intermittent fever, we are not any nearer the solution of the question relating to the *modus operandi* of the antidotes of malarial poisoning. For this medicine also acts powerfully upon the nervous centres of man; and indeed, a comparison of its physiological effects and of its germicide power indicates that the protoplasm of nerve-cells is more susceptible to its influence than is that of the low vegetable organisms of the class to which known disease germs belong.

The symptoms produced by toxic doses of carbolic acid are said to be "insensibility, feeble pulse, livid skin, and collapse. In cases that terminate favorably these symptoms are replaced by stupor, debility, a feeble pulse, cold skin, etc."[3]

The effects of a medicinal dose, "as for instance six to eight grains in a wineglassful of water, are the following: numbness followed by a sense of coldness in the mouth and lips; if the stomach is empty, nausea and an uneasy sensation in the abdomen, with vertigo, ringing in the ears, and slight deafness; the force and frequency of the arterial impulses decline, and sometimes diarrhœa occurs."[4]

The germicide power of carbolic acid has been determined for a considerable number of pathogenic organisms, and if we may reason from what is known with regard to its action upon these, it is safe to say that the hypothetical malarial germ would not be affected by the presence in the blood of medicinal doses of this agent.

According to Koch, a one per cent. solution destroys *Bacillus anthracis* very promptly; but to prevent the spores from developing requires exposure to a five per cent. solution for two days. The micrococcus of swine-plague multiplies abundantly in urine containing one per cent. of carbolic acid, while the micrococcus of fowl-cholera is destroyed by six hours' exposure to a one per cent. solution (Salmon).

In the writer's experiments[5] 0.2 per cent. added to a culture fluid was found to prevent the development of the test-organisms (*B. termo*, micrococcus of pus, and septic micrococcus). All of these organisms, however, multiply freely in the presence of 0.1 per cent. We may therefore assume that this amount present in the blood would not interfere with the development of pathogenic organisms. This would be about three-tenths of an ounce in an adult weighing 160 pounds. It is evident that the supposition that the phenomena of a malarial paroxysm are due to the presence of malarial germs in the circulation does not receive any support from the alleged curative power of this agent.

IODINE.—A more potent germicide agent than carbolic acid is iodine, but the reports relating to its curative power in intermittent fevers are not sufficiently favorable to give support to the germ theory of causation.

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[1] Centralblatt, Sept. 6, 1873.

[2] Indian Med. Gazette, April 1, 1874.

[3] National Dispensatory, p. 33.

[4] Op. cit.

[5] Am. J. of the Med. Sci., April, 1883

POTASSIUM BROMIDE.—Finally, we may refer to the alleged curative value of an agent recognized as a nervous sedative, but which is entirely without germicide power. We quote from a review of a paper by Dr. Moxon:

> It is known that bromide of potassium was first introduced into medical practice as a remedy for enlargement of the spleen by Dr. Williams. Reference to the cases which are given in full in his "Practice of Medicine" does not, however, show any relation of the remedy to ague poison more especially than other causes of enlarged spleen. It was as a spleen remedy and not as an ague remedy that it was found useful. During the last four months trial has been made at Guy's Hospital, among the out-patients, of the use of bromide of potassium in ague. The results are such as to show that this drug possesses a very remarkable power over ague, and a power that promises to be of important use in many of the more obstinate cases. Dr. Moxon has had several instances of its successful use; and two of these were in persons who had taken quinine for a length of time without benefit. . . .
>
> A considerable number of other more recent cases have been treated in the same way, and this has been the general result—that the bromide always checks the ague, so that for one or two weeks the patients have no seizures; that in some cases the cure is permanent, even while the patients continue to reside in the place where they took the ague; but that in many cases, when the patient is still in the ague district, the ague-fits return after one or two weeks of free interval.[1]

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[1] Braithwaite's Retrospect, Part lxii., p. 33.

CHAPTER VI.

PROPHYLAXIS.

General Prophylaxis.—The indications for preventing the evolution of malaria at its source are furnished by our knowledge of the conditions which favor its production. Of these conditions one—heat—is beyond our control. A second essential condition—soil-moisture—although it depends upon the amount of rainfall in the first instance, is largely within the control of man, and we have already referred to the notable sanitary amelioration brought about by subsoil drainage and improved agriculture in extensive areas in England, where formerly agues were of common occurrence, whereas they are now almost unknown. M. Colin says:

> Against a simple marsh, well defined and removed from the seaboard, or at least occupying a level notably superior to that of the sea, the efforts of an intelligent and persevering people will always triumph. Perhaps it will be necessary to pass at first through the most cruel proofs, and to add to the sacrifice of money that of many victims among the first laborers, but the prosperity of succeeding generations will attenuate the sad recollection; a population healthy and robust will replace the miserable types of its ancestors, and, as in our Normandy, and in a great part of Tuscany, the health of the inhabitants and productive richness of the soil will succeed long periods of decline and human misery.[1]

The opposite picture, viz., that of a fertile and populous plain becoming a pestiferous and deserted source of malarious exhalations, is furnished by the Roman Campagna. This plain, which at one time was called the granary of Rome, and over which numerous flourishing towns were scattered, under the devastating influence of civil war became depopulated. It was denuded of forest- and fruit-trees and agriculture was neglected. The result has been that it has relapsed into such a state of insalubrity that, according to Colin, "one sees at present but few cultivated fields, which it is necessary to harvest rapidly, precipitately, in order to remain as short a time as possible in the Campagna. It seems that each harvest is a theft made from this murderous soil, from which it is necessary to flee as rapidly as possible after having robbed it of the little which it still produces."

Next to thorough drainage and cultivation, the most important measure of prophylaxis as applied to the soil is, perhaps, the planting of forest-trees. The sanitary value of forests is probably due to several causes. They withdraw soil-moisture (see page 49), shade the earth and keep it cool, and perhaps prevent the evolution of malaria by consuming the organic pabulum in the soil upon which the malarial germs might feed. Trees also serve as a barrier against the noxious emanations of malarious lands when they are interposed between these and human habitations.

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[1] Op. cit., p. 462.

Practical sanitarians have of late years devoted much attention to the subject of the reclamation of malarious regions by the planting of trees, and the various species of *Eucalyptus* have been especially recommended for this purpose. It has been supposed by some that the aromatic oil which is contained in the leaves of this tree, which has some reputation as a remedy for the cure of intermittent fever, is an antidote to malaria, and being highly volatile may neutralize it in the atmosphere. No very satisfactory evidence of the truth of this supposition has been adduced, but that the eucalyptus may exercise a beneficial influence in malarious regions suited to its growth is beyond question. For this purpose its rapid and vigorous growth, and the large quantity of water which it withdraws from the soil, make it especially valuable. Unfortunately, however, it is very susceptible to cold, and the young trees especially are destroyed by a slight frost. It has been introduced quite extensively in Algeria and in the south of Europe, and the reports are favorable as to its value as a sanitary agent. The attempts to introduce it into India are said to have been almost a failure as far as the plains are concerned. "The seeds germinate and the plants grow rapidly *under shelter*, but they seem unable to bear the great solar heat and die when planted out."[1] The attempt to introduce this tree on the Roman Campagna has also been only partly successful. A correspondent of the *British Medical Journal*, located at Rome, in a letter dated June 21, 1880 (page 994), states that "when tended and planted in a carefully prepared soil the eucalypti thrive and grow most luxuriantly in and near Rome," but points out the difficulties and expense of starting plantations, and the fact that there are eight hundred square miles of more or less malarial Campagna. Also that almost every winter there are nights when there are "at least 6° Centigrade of frost on the Agra Romano." A note in the same journal of later date (January 1, 1881) is to the following effect:

> The singularly mild weather which has prevailed since October has been very favorable to the growth of the eucalypti in the Campagna. I lately had occasion to visit the monastery of the Tre Fontane, which is at present the chief nursery whence these plants are sent out. The monastery has of late years been in the occupation of French Trappists. From one of the monks I learned that the malaria which had hitherto at this spot been singularly pernicious has of late years become comparatively mild in type. This improvement is attributed entirely to the growth of the eucalyptus trees, which to the number of twenty-five thousand have been planted within the grounds of Tre Fontane. The shrubs are protected by wicker-work against injury during the first few years of growth, after which they are left to care for themselves. Those planted ten years ago have now reached a height of over thirty feet. The Trappists prepare a spirituous extract and an elixir from the leaves, both of which are strongly redolent of the odor and acrid taste of the eucalyptus. The extract they are accustomed themselves to take daily as a preventive rather than as a remedy for ague. When the attack is actually imminent, nothing is found to answer so well as quinine combined with some purgative. My informant was evidently himself thoroughly saturated with malarial poison, the virulence of which in this particular locality may be judged of by the fact that it proved fatal to all the eighteen friars who first attempted to plant the eucalyptus in the district. As it is, the health of the fraternity has so far improved that all thoughts of abandoning the monastery and the work have now been given up.

The eucalyptus grows luxuriantly on the Pacific coast of our own country, from San Francisco southward; but the writer has seen the young trees of one year's growth destroyed by frost on the Gulf coast, in the vicinity of Pensacola, Florida.

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[1] Report of Sanitary Commissioner of Madras Presidency, Med. Times & Gaz., Lond., Nov. 28, 1874, p. 610.

The application to argillaceous, malaria-producing soils of calcareous fertilizers—lime and marl—in connection with tubular drainage and thorough cultivation, is highly recommended by Béringuier as a prophylactic measure. This author has written an interesting work upon "the intermittent and remittent fevers of temperate and non-marshy countries," in which conditions relating to the soil in his field of observation receive special attention. This field of observation is the southwest of France, and particularly the sub-Pyrenean basin, where, Béringuier says, "periodicity rules the entire pathology. During a long time I have seen intermittent fever reign as sovereign, and, in a manner, absorb all the other affections."[1]

The sanitary benefit resulting from the liberal application of lime is believed by Béringuier to be due to the antiseptic power of this agent. He says:

> It is recognized that marl and lime produce remarkable effects upon lands newly cultivated in which there is present a great quantity of organic matter in decomposition. In effect, by the application of lime we introduce into the soil a caustic agent which serves to destroy the texture of organic material, the decomposition of which would otherwise have been very slow. . . . Upon the plateaus and in the river basins, where ordinarily the application of marl and lime is required, the soil formed by the superior layer of alluvium is of an argillo-silicious nature ; the subsoil is impermeable and supports a sheet of water which can only drain away with difficulty. In these conditions the superficial layer is saturated in winter, but during the summer season the sun warms the earth and drives away the water by evaporation. The diminution of moisture causes a concentration of extractive matters of all kinds with which the arable layer is permeated. Finally, when things are left to themselves fermentation is established, but if lime has been thrown upon these lands in sufficient quantity this fermentation does not take place ; the caustic agent destroys the material in decomposition and prevents the gaseous emanations which spread intermittent fever throughout the country.[2]

The flooding of malarious swamps and lowlands so as to cover them permanently with water is sometimes practicable, and when these lands cannot be reclaimed by drainage and cultivation is always desirable as a sanitary measure.

A like result is obtained when a malarious soil is covered with dwellings and pavements by the growth of a city. This is probably the main reason for the comparative exemption of the denizens of cities from malarial diseases. But another reason has been suggested by Dr. George B. Wood in his "Practice of Medicine," viz., that the products of combustion present in the atmosphere of cities may in some way neutralize malaria. Dr. Wood says:

> There is another extraordinary and very important fact in relation to miasmata which must not be overlooked. These effluvia are neutralized, decomposed, or in some way rendered innocuous, by the air of large cities. Though malarious diseases may rage around a city, and even invade the outskirts, where the dwellings are comparatively few, yet they are unable to penetrate into the interior ; and individuals who never leave the thickly built parts almost always escape. This fact is notorious in relation to the city of Rome ; and we have seen it abundantly confirmed in the larger towns of the United States in the neighborhood of which these diseases have prevailed. What it is in the air of the city which is thus incompatible with malaria is unknown, but very probably it is connected with the results of combustion ; for fire and smoke of camps are asserted to have the same effect, and I have been assured by persons inhab-

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[1] Traité des fièvres intermittentes et remittentes des pays tempérés et non marécageux, et qui reconnaissent pour cause les émanations de la terre en culture. Paris, 1865.

[2] Op. cit., p. 333.

> iting miasmatic districts of country that they have been able to protect themselves against the poisonous effects by maintaining fires in their houses during the sickly season.[1]

This suggestion of Dr. Wood's receives support from the alleged protection enjoyed by charcoal-burners in malarious regions. Thus Dr. Merideth says that "the charcoal-burners of different tea-gardens in Assam, who live near the pits and the charcoal, and who breathe an atmosphere strongly impregnated with the smoke and other products from the burning, rarely suffered from malarious complaints, and the cases of anæmia and etiolation were much less common than in other gangs of laborers."[2]

The same author gives another example of immunity from malaria among laborers employed at the petroleum oil springs at Marhum, in Upper Assam.

> The smell of petroleum is everywhere perceptible. Fifty-nine men, women, and children employed there for two years had only one death—an old woman. There was no anæmia, and cases of malarious fever were only occasional and were never protracted.[3]

There is also considerable evidence in favor of the view that sulphurous emanations neutralize malaria. This subject has recently been investigated by M. d'Abbadie, who has communicated the results of his investigations to the French Academy of Sciences.[4]

The facts collected by M. d'Abbadie relate to the comparative immunity from malarial diseases of the inhabitants of regions where all the conditions seem favorable to the production of malaria, but where sulphurous vapors are evolved from neighboring volcanoes, etc. The attention of this author was first attracted to the subject by hearing that certain elephant-hunters in intensely malarious regions in Africa enjoyed an immunity from the effects of the poison, which they attributed to daily fumigations of the naked body with sulphur. Recent observations at Stanhope, N. J. (Sussex County), give support to the conclusions of M. d'Abbadie. It is stated that since the furnaces located at this place began to roast sulphurous ores the town has been free from malarial fevers.[5] The writer has elsewhere suggested[6] that possibly the exemption which the Sandwich Islands are said to enjoy from malarial diseases is due to the fact that they are of volcanic origin, and that the largest active volcano in the world is located upon one of them. The immunity of the inhabitants of low coral islands may also be due, to some extent, to the calcareous nature of the soil. This would accord with the facts observed by Béringuier with reference to the prophylactic value of marl or lime when applied to an argillaceous, malaria-producing soil. Care must be taken, however, not to give too much weight to these facts relating to the nature of the soil or to the contiguity of active volcanoes in islands situated within the region of the trade-winds, for the purifying influence of these ocean breezes is a factor which cannot be ignored.

The experience of physicians in malarious localities in all parts of the world supports the popular idea that the night-air is especially dangerous, and that the danger of contracting a fever is greater near the ground than at a slight elevation above it. Hence it is that strangers are earnestly cautioned in such regions to keep their doors and windows closed at night, to sleep as far from the ground as practicable, and not to expose themselves out of doors after sundown or before the morning sun has dissipated the vapors which accumulate near the surface of the ground during the night. The value of this precaution is well illustrated by the facts related by Dr. John Ward with reference to the immunity from malarial fevers of the insane inmates of the New Jersey State Lunatic Asylum. Out of 672 patients not one suffered from malaria, while several laborers and attendants did. The explanation given is that the patients were not allowed out of doors after nightfall.

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[1] Op. cit., vol. i., p. 161.

[2] Report English Army Med. Dept., 1870, Appendix, p. 239.

[3] Op. cit.

[4] Comptes Rendus, t. xcv., pp. 497–500.

[5] Gaillard's Med. Journal, Nov. 3, 1883.

[6] Sanitary Engineer, New York, Jan. 11, 1883.

M. Colin, who has devoted more than seventy pages of his valuable work to prophylaxis, insists strongly upon the importance of avoiding the night-air in malarious localities. He says:

> All the villages which border upon the peripheral zone of the Roman Campagna are situated upon the heights, where each evening the laborer can come and hide himself from the empoisoned air of the plain. For the same reason, during the season of fevers the inhabitants of Rome and of Civita Vecchia, and of all the centres surrounded by a dangerous zone, rarely leave the city at night. . . . Recently, in France, this danger of exposure at night has been pointed out by MM. Pécholier and Saint-Pierre with reference to some industries upon the banks of the Lez, near Montpellier: "In a general manner, and without regard to the nature of their occupation, the day-laborers—that is, those who returned home at night—were much less subject to be attacked than the workmen who slept in the workshops." . . . Puvis has traced a striking picture of the poor little shepherds of the Dombes, who pass the nights in guarding their flocks, exposed without resistance to the full activity of the miasm. . . . How often have the precepts of Lind been confirmed, who opposed with the greatest energy debarkations at night upon an insalubrious coast.

INDIVIDUAL PROPHYLAXIS.—It is very generally believed by those who have had much experience in malarious regions, that exposure while fasting is especially dangerous. Hence those in charge of troops or of laborers in such regions are accustomed to issue coffee or spirits to those men who are required to go out for guard duty or for work of any kind before breakfast. A good cup of coffee is decidedly better than a spirit ration under these circumstances, and it is probable that coffee has some prophylactic value aside from its supporting and stimulating properties when taken hot. The issue of a spirit ration in the early morning may be justifiable under certain exceptional circumstances of exposure, but the writer's observations lead him to believe that the daily issue of such a ration to troops in a malarial region does more harm than good. The appetite for strong drink is rekindled in those who have at some time in their life been addicted to the immoderate use of spirits, and young men learn to look upon this as a cure-all for heat, cold, fatigue, or hunger, and thus fall into intemperate habits. The morning debility following a night of debauch is a condition especially favorable for the action of the malarial poison, as is also the debility resulting from extreme fatigue.

No doubt exposure to the damp night-air, aside from the presence of malaria in such an atmosphere, is often the immediate cause of a paroxysm of intermittent fever. The unsettling of nervous equilibrium which results from chilling the surface of the body has this special result in individuals who are under the influence of the malarial poison. For this reason it is important, when exposure at night is unavoidable, that extra precautions be taken to avoid chill by the use of warm clothing. Several authors insist upon the wearing of flannel underclothing in malarious regions, and this is no doubt good advice.

In general, those who are best housed, best clad, and best fed are best able to resist malaria. M. Duboué has said: "Malarial infection is rare among the wealthy (*la classe aisée*). Eight-tenths of the cases of malarial poisoning which I have observed I have seen among the very poor or those of restricted means, and the few examples that I have noted among the rich have almost always been explained by hygienic imprudence."[1]

The prophylactic value of quinine has been denied by Professor Sée and others, but the experience of our own army surgeons during the late war, and of the English medical officers in India, amply demonstrates its preventive power when properly administered. A valuable brochure by Dr. Stephen Rogers, Surgeon of the Seventh New York Regiment, and formerly surgeon to the Panama Railroad Company, was published during the second year of our civil war, and doubtless did much good by calling the attention of medical officers to this subject.

Dr. Rogers states that while on the Isthmus of Panama, where he was constantly exposed to malarial emanations, he did not suffer a single attack of malarious disease, and this immunity is attributed entirely to the use of quinine. This author agrees with Colin in considering a single attack of remittent fever, or "first miasmatic fever" as he calls it, as protecting to a great extent from future attacks. He says: "A species of toleration of the surrounding influences is acquired, lessening the impression of the poison upon the sensorium, so that after more or less time, aided perhaps by a depression of the powers of life and consequent want of vital force to sustain a violent contest, the intense and destructive action of the fever ceases to occur."

This acclimating process, Dr. Rogers believes, may occur when the patient is kept under the influence of quinine, without the patient passing through the ordeal of an attack of this "first miasmatic fever." The longer the attack is postponed the milder it is said to be, and by the systematic use of quinine it may be prevented altogether. Dr. Rogers' experience leads him to believe that "doses too small to produce a sensible and decided impression upon the nervous system cannot be depended upon." Four grains administered twice daily were usually sufficient, and in some cases three answered the purpose. Others, again, required more, and it was necessary to regulate the dose according to the effect. These doses our author does not hesitate to continue for thirty days or more. He says:

> The rule then for all cases is, when men are about to be exposed to miasm give them from three to five grains—according to known effect—before exposure, and repeat the dose once in *twelve* hours, during the whole period of exposure, up to about thirty days in the *permanent* resident; extending it even to sixty days in the *transient* resident, where there are peculiar reasons for desiring to avoid subsequent miasmatic disease; not forgetting that cases often occur wherein it will be necessary to repeat the dose once in *eight* hours to keep up the required *quinine effect*, which is our only certain guide, and is to be carefully watched and maintained in all cases. Another rule is, no quinine is required after exposure ceases.

As further evidence of the prophylactic value of quinine we quote from a communication to the *Boston Medical and Surgical Journal*, dated Newbern, N. C., September 10, 1863, and signed by Dr. George Derby, Surgeon Twenty-third Massachusetts Volunteers:

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[1] Colin, op. cit., p. 517.

First, as a prophylactic. My own belief is that quinine so perfectly antagonizes the fever-poison that, except to those who have previously suffered from the effects of malaria, the protection is complete. The inhabitants of malarious districts, those who have been born and bred in a fever country, cannot be completely protected. They get a habit of shaking which is revived by every exposure at certain seasons. Those of our Northern soldiers who once get chills and fever are never afterward entirely safe in certain places and under certain conditions. The conviction at which I have arrived, and which is so strong that I would, if an opportunity occurred, test it by passing a sufficient time on a rice plantation, is founded upon the observation of many facts, some of which I am able to give you.

During the summer of 1862 I lived in a house in Newbern with several other medical officers. We each took two grains of quinine daily, from about July 1st till frost in November. No one suffered from periodic fever. One of our number was detailed to go to Roanoke Island in September, to assist the surgeons there, who were overworked. He remained there five weeks, in a region steeped in miasma, taking daily four grains of quinine, instead of two as at Newbern, and maintaining perfect health throughout the whole period, and to the present time.

During the summer and autumn of 1862 the Twenty-third Massachusetts Regiment was doing guard duty in Newbern. In each of the company quarters was placed, in charge of a sergeant, a solution of quinine in water, with a little aromatic sulphuric acid, and a recommendation from the surgeon that each man should take a certain amount, equal to two grains, daily. In this way enough was used to make it evident that about half the whole number of men took it daily. The sick-list was remarkably small throughout the whole period.

June 21st, 1863, a company of fifty-nine men, with two commissioned officers, was placed in Fort Spinola, one mile below Newbern, on the bank of the river. From that time till August 21st, when they were removed, every man, except fourteen, took two grains of quinine daily in watery solution. During the first two weeks these fourteen men refused to take it, and after that period I refused to give it to them unless they were sick. Of the fourteen, eight had either remittent or intermittent fever. Of the remaining forty-seven men and two officers, the prescriptions show that only seven required quinine as a remedy, and of this number one had chills before coming there and others were exposed during the previous summer and autumn.

Dr. J. B. Hamilton, Royal Artillery, states that he has had numerous opportunities in the East and West Indies, and in Central America, of testing the value of quinia and its allied drugs as prophylactics where malaria is present.

In Jubbulpore, in the East Indies, Dr. Hamilton had the care of a battery of the Royal Artillery, and he gave the men under his charge two grains of quinia each, with marked benefit, during the months of September and October, 1865. In 1866 a regiment of the line arrived at the same station, and, as the surgeon of the regiment did not believe in the prophylactic powers of quinia, the alkaloid was not administered to the men, although Dr. Hamilton continued to give it to his battery. The wet season of 1866 happened to be a very malarious one, and fever of a severe remittent type attacked the regiment, one hundred and fifty men being in hospital out of a force of five hundred, and about twenty deaths took place. During the same time the health of Dr. Hamilton's battery remained remarkably good, only about four per cent. being in the hospital, and no deaths occurring. Ever since that year Dr. Hamilton has carried out the same plan, and last year he made some comparative experiments as to the value of quinia, cinchonia, and quinoidia, and the result was that he placed cinchonia first as a prophylactic, then quinia, and at a long interval quinoidia. He finds that by the prophylactic plan the cases of fever are fewer, of a milder type, and more amenable to treatment, while the sequelæ, such as dysentery, enlargement of the spleen, etc., are very rare.[1]

Tommasi-Crudeli has recently been experimenting with reference to the prophylactic value of arsenic, and has obtained results which he considers encouraging. He has administered this agent to a large number of individuals exposed in malarial localities, and has had exceptional advantages for making a careful study of its value, as the railway officials have co-operated with him. The arsenic was administered in thin gelatine tablets, with which it was incorporated in such quantity that each one contained exactly two milligrammes. One of these tablets was given daily, and usually the dose was increased until a maximum dose of four was reached. The experiment is an interesting one, but whether arsenic possesses any advantages over quinine other than its cheapness is extremely doubtful. A report based upon more extended observations is promised at some future time.[1]

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[1] Indian Med. Gazette, Nov., 1871.

The author last quoted has not found the alcoholic preparations of eucalyptus of any special value as a prophylactic.

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[1] La préservation de l'homme dans les pays à malaria. J. d'hyg., Par., 1883, viii.

CHAPTER VII.

GEOGRAPHICAL DISTRIBUTION.

The extended literary researches of Hirsch, and the concise statement which he has given us with reference to the geographical distribution of malarial diseases in his "Handbook of Geographical and Historical Pathology," makes it unnecessary for the present writer to attempt to define the territorial limits of malarial evolution. But as the valuable work referred to will not be accessible to many of the readers of the present volume, we quote this chapter *in extenso* from Dr. Creighton's translation, recently published in London by the Sydenham Society.[1]

Africa.—First and foremost, we meet with one of the most intense malarial regions of the eastern hemisphere in *the tropical part of the continent of Africa* and the islands adjoining thereto. In the *basins of the Senegal and Gambia* the disease is enormously frequent and malignant, equally on the marshy coasts and river banks and in the relatively dry regions of the upper river basin. Next, over the whole *Guinea coast* from Sierra Leone down to Cape Lopez, but more especially in the basins of the Niger and the Gaboon; and, further, on the coast of Sierra Leone, the Ivory and Gold Coasts, and the adjoining islands of Fernando Po and St. Thomas.

There is better health from Cape Lopez downward, and along the *Congo coast*, where the regions of more intense malaria are met with only at intervals, as in the swampy neighborhood of Benguela; and this exemption from malarial disease becomes more and more marked the nearer we approach the *Cape of Good Hope*, which itself enjoys, along with *St. Helena*, an almost complete immunity from endemic fever. The same exemption obtained, up to a few years ago, in the islands of Reunion and Mauritius, situated within the tropics; but since 1866 centres of intense malaria have developed in these colonies under the circumstances to be afterward mentioned.[2]

A second great malarial region of the African continent is formed by the *east coast* from Delagoa Bay upward along the littoral of *Sofala*, *Mozambique*, and *Zanzibar*; the trustworthy accounts of travellers place it beyond doubt that the foci of malaria there extend far into the interior, from the shores of the Zambesi, Schiré, and Rovuma, and beyond Lake Ngami to the northern border of the Kalahari Desert. Not less common and pernicious is the disease in the *Comoros* and in *Madagascar*, where the northeast coast only and the mountainous part of the interior enjoy more favorable conditions of health. The extensive plateau of *Somali Land*, owing to its generally elevated position, the dryness of the soil, the absence of swamps on its thinly wooded coast, and the circumstances of its climate, probably deserves the character for comparative healthiness which certain travellers have given it. Also in those parts of *Abyssinia* that are subject to the same influences, malarial diseases occur only to a moderate extent and of a relatively benign type. This holds good for the strip of coast (mostly narrow', with the exception of a few marshy points, such as Massowah (which is almost uninhabitable for Europeans on account of its malaria), as well as for the whole *west coast of the Red Sea* generally, and it holds good also for the Abyssinian highlands; while malarial diseases are endemic in their most pernicious forms in the narrow, densely wooded, and damp river valleys, in the swampy flats of Seraë, Lower Samen, etc., as well as on the shores of the Takazzé and Lake Zuaie.

The countries of which we have just been speaking form the eastern portion of a third great malarial region, which extends from the western slopes of the Abyssinian highlands across *Nubia*, and a great part of the Soudan (as much of it as is known), and through the marshy flats of *Kordofan* and *Darfur* as far as Lake Tchad (whose shores are the seat of the worst kind of fever), and probably beyond it as far as the elevated plains to the west. In Nubia the chief endemic seats are the banks of the two arms of the Nile, more especially *Khartoum*, situated at their confluence, and the Nile valley from that point down to Dongola. Then comes a region free from malaria, including the northern parts of the Dongola Steppe and the rocky plateaus of that country, as well as *Upper Egypt* and the greater part of *Middle Egypt;* that, again, is succeeded by a malarial zone which includes the low-lying province of *Fayoum*, in direct connection with the Nile valley, and follows the river from Cairo to the shores of the Mediterranean, becoming broader as it advances northward, and extending more particularly over as much of *Lower Egypt* as is watered by the Nile.

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[1] Vol. i., Acute Infective Diseases, pp. 198–228.

[2] See page 17 of present volume.

In *Tripoli* the basin-shaped province of *Fezzan*, abounding in salt lakes, together with the oases, is stated to be the seat of pernicious endemic malarial diseases; in *Tunis* also they are prevalent under the same circumstances. Finally, we meet with a very extensive region of malaria on African soil in *Algiers*. The coast zone is here the headquarters of the disease. Among particular coast localities there are: in the province of Constantine, Bona, Philippeville, and Gighelhy; in the province of Alger, the plain of Metidja, Alger, Blidah, Koloah, and Tenes; in the province of Oran, Mostaganem, Oran, Ain-Temouchen, and others. But malarial diseases are also widely spread on the uplands of the Greater and Lesser Atlas, on the banks of the Seybus, in Constantine, Setif, Batna, in Medeah, Milianah, Teniet-el-Had, Tiaret, Mascara, etc., and in many oases of the Great Desert, such as Biskara, Tuggurt, Ouaregla, and Lagouat. From those disease-centres we pass to the great malarial region of the Soudan. According to an approximate calculation, the yearly number of admissions for malarial diseases among the French troops in Algiers amounts to about one-half of the admissions for all diseases whatsoever occurring among them.

Asia.—We come next to the malarial regions of the tropical and sub-tropical parts of the *Asiatic continent* and the islands belonging thereto. Among these *Arabia* takes a prominent place. In contrast to the western shore of the Red Sea, which is little infested by malaria, there is a region of very considerable malaria in the flat marshy strip of coast of the Hedjah (especially at Jeddah and Yembo), and in Yemen from Jisan downward to Mocha. Aden, situated at the southern extremity of this coast, is free from endemic malarial fever; and from the accounts of travellers the sandy plateau of the interior should also enjoy favorable sanitary conditions. On the other hand, the disease prevails in its worst forms on the south coast, especially in Muscat, along the marshy shores of the Persian Gulf and the adjoining islands, as well as in a wide-spread endemic in the valleys of the Euphrates and Tigris, from their mouths upward throughout *Mesopotamia*.

In *Syria* we meet with extensive regions of malaria in the damp valleys of the Lebanon (equally in the valley of Beka, situated at a height of 1,200 metres, and in the valley of the Jordan near the Dead Sea); further, at Jerusalem, Damascus, Aleppo, and other inland places, but especially in the coast localities, in Gaza, and up the coast to Jaffa, Tyre, Sidon, Beyrout, Tripoli, Acre, and Skanderoum. From these centres the malarial region extends to the soil of *Asia Minor*, from Adana and Tarsus along its south and west coast (including Smyrna), the marshy banks of the Scamander, the plain of Troy, and along the coast of the Black Sea, from Sinope around the Gulf of Iskimio and Broussa to the Dardanelles. The accounts of travellers are too slight to enable us to say how far inland the disease is endemic.

The table-land of *Armenia*, with the exception of a few points, and the central mountainous region of *Trans-Caucasia*, are little subject to endemic malaria; on the other hand, it is prevalent to a great extent on the marshy steppe of the Kuban, in the damp valleys opening toward the Black Sea, on the banks of the Terek, especially in the neighborhood of Kisljar, in low-lying places in Dagestan, but in its very worst forms in the valleys of Abchasia, Mingrelia, Guria, and Imeretia, in the valley of Alasan, on the Mugan Steppe, on the banks of the Kura as far as Lenkoran, as well as in the plain watered by the Araxes. From that point the malarial region extends along the marshy shores of the Caspian to *Persia*, where endemic malaria is met with in the provinces of Ghilan and Mazenderan, in the valleys of the Attrek and Gurgan, opening toward Turkoman territory, at several points on the plateau of Teheran, but of the most pernicious kind on the shores of the Persian Gulf, especially in Bushire.

Among the more considerable malarial regions of the continent of Asia we have to include *Beloochistan* and *Afghanistan*. The endemic fever is met with in these countries equally on the swampy coast margins, as in Seistan, abounding in salt marshes, in the lofty and dry Kelat, in the marshy plain of Dedar, and in the Bolan and Kandge Passes branching from it, and, further, in Kandahar and in the mountain valleys of

Cabul and Jelalabad. The last of these joins on to the great malarial region which extends over the northern plain of Hindostan, from the Punjaub through Sind and part of the Bombay Presidency, the Northwest Provinces and Bengal corresponding respectively to the valleys of the Indus and Ganges. . . . A point of especial interest for the history of malarial diseases in India is raised by its occurrence on the *table-land of the Deccan*. These fevers occur even in the mountainous countries of Chota Nagpore and Gondwana, sloping on the east toward Orissa and on the west joining on to the Vindhya Mountains, and there forming the boundary between the Deccan and the plain of Hindostan; and it is not only in the alluvial valleys that the fevers occur, but also, under the name of "hill-fever," on the absolutely dry soil of elevated points. It is these very hill-fevers that make up the greater part of the endemic malaria of the *Madras Presidency*. The coast belt of that Presidency, perfectly flat, and for the most part sandy and scantily watered, is the part least affected, the disease being met with only at several scattered points, . . . where artificial irrigation, canals, or jungle plantations exert an influence special to the locality. . . . The Malabar coast and all the western littoral belonging to the *Bombay Presidency* is much more unhealthy than the east coast. Here also there is only a narrow margin of plain, but it is richly watered. abounding in woods and brackish lakes, marshy in part or subject to periodical inundations, and therefore extensively malarious except at the more elevated and dry localities. . . .

Among Asiatic countries in which malaria is severe we have further to include *Ceylon*. The disease in that island is endemic not only on the coast, but also in the mountainous regions of the interior. . . . Another malarious territory is formed by the richly watered plains and the hilly countries of Lower India, where the fevers occur endemically in their severest forms. . . . Endemic foci of malaria are met with also in wide distribution throughout the *Indian Archipelago*, especially in the *Nicobars*, on the western and southern coasts of *Sumatra* (particularly Singkel, one of the unhealthiest places in the tropics, Padang, and the Bay of Pulo), in *Banka* and the small islands near it, in *Java*, especially its northern and western coasts, in *Bali*, in *Borneo*, especially on the east and south coasts, and to a lesser extent on the west, on the east coast of the *Celebes* and in the *Moluccas*, particularly Amboina, where a focus of intense malaria has developed in more recent times; the *Andaman Islands* belong also to the malarious spots of this part of the world. On the other hand, we have to note certain points which enjoy a comparative immunity from malarial fever, such as the north coast of the *Celebes*, *Ternate*, the flat banks of the Palembang in *Sumatra*, the archipelago of *Riouw-Linga*, and *Manilla*.

Australasia and the Pacific.—An extremely interesting contrast to this wide prevalence of endemic malarial disease in India and the Indian Archipelago is afforded by the state of matters in the *Australian Continent* and throughout Polynesia. Truly endemic seats of malaria are met with there on the coast of *New Guinea*, according to the accounts of Dutch physicians, but nowhere else. Cases of malarial fever are said to have been often observed also in some of the small island groups, such as the *New Hebrides* and the *Tonga Group*. The continent of *Australia*, again, so far as it has been settled by Europeans, particularly its southern and eastern coasts, with *Tasmania*, enjoys an almost complete immunity from those diseases; and that applies also to *New Zealand*, according to the unanimous reports of observers, as well as to *New Caledonia* and the *Fiji*, *Samoa*, *Wallis*, *Society*, *Gambier*, and *Hawaiian Islands*. Brunet, who lived for five years in various parts of Oceanica, states that he did not observe a single case of malarial fever during that period.

China and Japan.—The last malarial region on the continent of Asia, and one of the most intense, is met with in the tropical and sub-tropical parts of *China*. Not only are there foci of malaria on the coast, among which Macao, Hong Kong, Canton and neighborhood, Tai Wan (Formosa), Chee Foo, Shanghai, Chusan, and Tien Tsing may be mentioned as especially unhealthy, but they exist also in the interior, where, as Wilson states, the disease occurs along the course of the rivers as extensively and in as severe forms as on the coast, and where, as he adds, it exerts an influence more pernicious than in the malarial regions of India. . . .

As to the endemic occurrence of malarial fevers in *Japan*, there are merely occasional notices from Nagasaki, Yokohama, and Jeddo, and more particularly from the islands of Sikokf and Kiushiu, situated in the south; but it would appear that the disease occurs only to a moderate extent and in its milder forms.

Respecting other countries on the continent of Asia situated within temperate or cold latitudes, there are only a few references to the occurrence of malarial diseases at certain places in *Siberia*, such as the mines of Smeinogorsk (51.9° N.), Barnaul, and the Barabinsky Steppe, which abounds in marshes and salt lakes.

Europe.—From the point last mentioned, which joins on directly to the Kirghiz

Steppe, we pass to European soil by way of *Russia in Europe*, and therewith enter upon a wide region of malaria, which extends from the steppes of Asia to the steppe-lands of the Caspian, follows the course of the Volga through Astrakan, and includes the central Caucasian plain and the countries bordering on the Black Sea on the north, *Taurida*, the *Crimea*, with the notorious valley of Inkermann, *Cherson*, and *Bessarabia*, the basins of the Dnieper and Dniester as far as *Ekaterinoslav*, the *Ukraine*, and *Volhynia*, as well as *Moldavia*, *Wallachia*, *Bulgaria*, and *Hungary*, forming the Danubian basin. The malarial fevers prevalent throughout this great territory are well known under the various names of Dacian, Taurian, Crimean, Wallachian, and Hungarian fever, and they have been long of evil repute; even at the present day they may be met with throughout many of the above-named regions in their old pernicious form.[1]

A second and less important malarial region of *Russia* extends from Volhynia across the marshy level of Western Russia. . . . Coming to *Poland* I find more particular accounts of endemic malaria only for the Government of Augustowo, which has very numerous lakes.

In *Galicia* also we find endemic foci of malaria in only a few of the smaller districts, especially in the hilly northern part of the country, covered with marshes and ponds, . . . while the southern part of the country, rising in terraces toward the Carpathians, is little affected by the disease. A like exemption from malarial disease is enjoyed by the southern slopes of the Carpathians. It is when we descend into the plain that we come upon one of the largest and most notorious malarial regions of Europe, following the course of the Danube and its tributaries from the plain of Lower Austria, extending on both sides of the river over a great part of Hungary, through the low country of Slavonia and Croatia, as well as through Banat, Syrmia, and the Danubian Principalities, and joining on directly, as we have seen, to the great malarial region of Southern Russia. . . .

In the *Balkan Peninsula* we meet with foci of endemic malaria in many parts of *Roumelia*, on the *shores of the Black Sea* and of the *Sea of Marmora*, in *Albania*, and upward along the coasts of *Dalmatia* and *Istria*. . . . As regards *Greece*, we are assured of the endemic occurrence of malarial disease at many points. . . . In *Crete* endemic malaria is very common, as it is also in several of the *Ionian Islands*, particularly Cephalonia, St. Maura, and Corfu; while *Malta* enjoys a complete immunity from malaria except in a few isolated centres near the marsh of Puales and the frequently inundated La Marsa.

In the *Apennine Peninsula* there are especially two great regions that form the seats of endemic malarial disease—the *Plain of the Po* and its tributaries, and the *west coast* from Pisa down to and including most of Calabria. The first of these begins in the low-lying parts of *Piedmont*, . . . and extends thence through the *Plains of Lombardy and Venetia*, following the course of the Po, etc. . . . The second great malarial region of Italy, that of the west coast, begins with the marshes on both sides of the Arno, near its mouth, extending from Pietra Santa downward by Pisa to Leghorn. To the south of Volterra and Siena the district merges in the *Tuscan Maremma*, which extends to Civita Vecchia. This plain, bounded on the east by the slopes of the Apennines, contains hardly any marsh, and is for the most part dry and barren, but it is notorious for its endemic malaria, which is at its worst in the province of Grossetto. At Civita Vecchia, itself a hot-bed of malarial fever, the Maremma merges in the *Campagna di Roma*, which, together with the city of Rome, forms one of the chief seats of the disease.

Next come the *Pontine Marshes*, extending along the foot of the hills from Velletri to Terracina, and lastly the malarial region of the *Neapolitan west coast*. . . . Endemic malaria is widely diffused in *Sicily*, not only on the coast or in the plains, but also in the elevated districts. The same applies to *Corsica*, especially the east coast, and to *Sardinia*. For the *Iberian Peninsula* I am able to adduce only a few general facts about endemic malaria, owing to the absence of more particular accounts. The fevers occur in their severest forms and to the greatest extent in the southern and western coast regions, in the low country of Andalusia, on the marshy banks of rivers, especially the Guadiana and Guadalquivir, as well as the flooded plains of the Tagus, Sado, Mondego, and other coast rivers of Portugal, on the level coast of Granada and Murcia, and the plains of Algara and Alemtejo. Next in frequency and in less severe forms it occurs on the dry table-lands of Castile and Estremadura. . . . Gibraltar, built on rock, enjoys an almost absolute immunity from malarial diseases. . . . It remains to mention the *Balearic Islands*, especially Majorca, as a region severely infested by malaria.

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[1] We remark that the malarial fevers described by many of the authors upon whom Hirsch has been obliged to depend for the general account which he has given us, doubtless correspond with the "continued malarial fevers," not curable by quinine, which we have referred to in the Introduction to this volume, and which we suppose to have a different etiology from the periodic fevers properly designated malarial. This is especially true of the "pernicious malarial fevers" above referred to under various local names.

On *French* soil endemic malaria, apart from its prevalence at numerous isolated spots on the damp banks of rivers or in deeply cleft, waterlogged mountain valleys, is limited more particularly to the western and southern parts of the country. The western region of malaria begins in the lower basin of the Loire, and extends to the mouth of the Adour, or to the foot of the Pyrenees. Upward from the Loire mouth the endemic habitat extends on both sides of the river through Nantes, Angers, the arrondissements of La Flèche and Duretal as far as Tours, thence through the Sologne country to the swampy plain of *Brenne* in the basin of the Indre, not less celebrated than the Sologne for the deplorable ill health of its inhabitants. The endemic region at the mouth of the Loire connects with that of the Vendée, the marshy soil of *Charente inférieure* (including the long-known malarial centres (*marais salantes*) of La Rochelle, Rochefort, Brouage, St. Agnant, and Marennes), the *Gironde*, and lastly the plain of *Landes*, where the malarial region extends westward to Nerac and southward to Dax and Bayonne, or to the slopes of the Pyrenees and the banks of the Adour.

The second great malarial region of France stretches along the *coasts of Languedoc and Provence*, with their numerous lakes and marshes. The disease begins to show itself prominently in Narbonne, Bézières, Cette, Montpellier, and Nismes, but the endemic fevers reach their highest point, whether as regards extent or severity, in the Rhone delta, on *Camargue*, and in the level country on both sides of the river mouth. . . . Up the Rhone also, as far as the confluence of the Ardèche, malarial diseases are widely spread; and we meet with still another and larger centre of them at the confluence of the Saône in the marshy plains well known by their names of *Lombes* and *Bresse*, which stretch away from Lyons between the Saône and the Ain. . . .

In *Switzerland*, where there were formerly many small spots of endemic malaria in damp river valleys (of the Rhine, Linth, Reuss, etc.), and on the shores of lakes (especially the lakes of Zurich and Lucerne), the disease occurs now endemically at only two points, in the southern part of the Canton Ticino and in the Canton Vallais along the Rhone, especially from Sion to its inflow into the Lake of Geneva.

In the southwestern parts of *Germany* we meet with small and narrowly circumscribed foci of the disease on the marshy banks of rivers or lakes and in damp mountain valleys (as in the side valleys of the Neckar in the Black Forest); but besides these there are larger malarial regions *on the banks of the Rhine* (in Lower Alsace) in the Palatinate and the Rheingau, and in the *low grounds of the Danube* and its side valleys in Würtemberg and Bavaria. In *Austria* it is again along the Danube that we find the chief seats of endemic malarial disease, although there are also smaller malarious spots in the river valleys of Upper Austria, Salzburg, Styria, and Carinthia. Where the river widens out at Krems we come upon that great region of disease which extends, as we have seen, along its shores to the Black Sea. In *Central Germany* the disease as an endemic is confined to a few small districts. In the plain of *North Germany*, on the other hand, it is much more widely spread, being found in the basins of the Vistula, Oder, Elbe, Weser, and Rhine. The prevalence of malarial diseases is not inconsiderable even in the *delta of the Vistula* in *Lower Silesia*, and at a few places in the *Mark* of Brandenburg and in *Mecklenburg;* but it reaches its maximum, both of extent and severity, in the western coast districts of *Holstein* and *Schleswig* (especially Dittmarsh), on the coast belt west of the Elbe, the moorlands of *Hanover* and Oldenburg, the damp and in part waterlogged low grounds of *Westphalia*, and in the plains of *Rhenish Prussia* bordering the Rhine and its tributaries.

This malarious region of the plain of Germany is continued without break across the *Netherlands* frontier, where the disease is mostly found in the provinces of Grönland, Friesland, and Zeeland with their brackish marshes (the so-called "polders"), and in the coast belt of the provinces of North and South Holland; it is endemic also in the provinces of Drenthe and Overyssel, and in fact no province of Holland is altogether free from it. This malarial area on the west coast of the country merges in the endemic fever region of the low-lying parts of *Belgium*, particularly West Flanders with its numerous marshes, and also East Flanders and Antwerp, whereas the elevated and dry provinces of Brabant, Namur, Liege, and the like, are little affected by malaria, and the mountain districts proper are quite free from it.

The *British Islands* enjoy a very notable immunity from endemic malarial disease, particularly *Ireland* and *Scotland* (which is now, at least, quite free from it) and the *northern counties of England* and *Wales*. The only localities in which the disease is endemic to any considerable extent occur on the *east coast*, including the *East Riding* *of Yorkshire*, the counties around the Wash noted for their fens (Lincoln, Huntington, Cambridge, and Norfolk), where, however, the fever has lately decreased to a great extent, and the counties of *Essex* and *Kent*. In the rest of England we meet with only isolated and narrowly circumscribed spots of malaria, mostly associated with damp and waterlogged river banks, as on the banks of the Thames in Surry, and in the south marsh of Somersetshire.

In the islands of the kingdom of *Denmark*, where malarial fever was formerly reckoned among the prevalent diseases, it now occurs as an endemic sickness only on the islands of Laaland and Falster. It is still met with in *Norway* as an endemic on the Hvalöer Islands and in the neighborhood of Frederikstad. In *Sweden* the foci of malaria appear to have increased considerably in extent and in number in recent years. The disease is found as an endemic at three principal points; in the central depression of the country around the shores of the great lakes, especially Lake Mälar and Lake Wener, the most northern limit of its diffusion there being the Hedemora district in 60° 20′ N. . . .

Malarial fever is not endemic in *Finland*, nor has it been observed in the *Faröe Islands* or in *Iceland* apart from imported cases.

In the *Western Hemisphere* endemic malarial fever of the severest type has its principal seats in the West Indies, on the Mexican Gulf coast, and in Brazil; but considerable regions of fever, though of a less intense kind, are met with in the northern parts of the Pacific coast of South America, and in the southern, central, and prairie States of the Union.

West Indies.—Among the *West India Islands*, those chiefly affected by malarial sickness are Cuba, Jamaica, San Domingo, Guadaloupe, Dominica, Martinique, Sta. Lucia, Grenada, Tobago, and Trinidad; while others, such as Antigua, St. Vincent, and Barbadoes, enjoy a relative immunity, and the last of these is even in high repute as a sanatarium for patients with malarial sickness. In the *Bahamas* malarial fever is comparatively rare; in the *Bermuda* group it is almost unknown.

South America.—One of the worst centres of malaria is on the *east coast of South America*, including the very unhealthy ports of Carthagena, Maracaybo, and Puerto Cabello, and the ill-reputed country of *Guiana*, where the fever is a terrible scourge to the inhabitants, not only on the coast, but also, and even still more, on the inland plains and in elevated situations.

A region of less intense but very widely spread malaria covers almost the whole of the *north of Brazil* as far down as Rio de Janeiro; and here also the disease is equally prevalent in coast localities and elsewhere—on the flat and often inundated banks of the Amazon, Rio Madeira, Maranhão, etc. . . .

There are also widely diffused endemic foci of malaria in the *prairie lands* (pampas) of *Paraguay* and *Bolivia*, particularly in the provinces of Tucumana, Salta, and Santa Cruz. The circumstances are decidedly more favorable in the southern provinces of Brazil, San Paulo and Rio Grande do Sul, and that applies still more to *Uruguay* and the eastern provinces of the *Argentine Republic*, which, according to the unanimous verdict of observers, enjoy an almost absolute immunity from malaria. On the Pacific coast of South America, *Chili*, which was formerly quite exempt from malaria, has been visited since 1851 by pernicious epidemics, and at a few points in that country the disease has assumed an endemic character; but the proper region of severe endemic malaria does not begin before *Peru*, where the disease occurs very abundantly and in severe forms equally on the coast and among the deep eastern valleys and spurs of the Sierras. The endemic sickness extends thence along the coast to *Ecquador*, and probably also to *New Granada*; in the eastern parts of Ecquador, especially in the districts within the upper basin of the Maroñon, malarial diseases are said to be rare.

Central America.—In the countries of *Central America* the malarial diseases have their chief seat on the Atlantic (Gulf) coast from Chagres up to Cape Garcias a Dios, and on the interior plain up to the height of 600 metres. The Pacific coast is less severely visited, although there also endemic foci of malaria are met with, particularly in Corinto (port of Nicaragua), on the coast of San Salvador, and in the valleys of the Lempa and St. Miguel, as well as on the coast of Guatemala. In *Mexico* also it is on the Atlantic coast that malaria predominates, as in several ports of Yucatan (Balize in British Honduras, Sisal, and Carmen), on the coast of Tobasco, in Alvarado, Sacrificios, San Juan d'Ulloa, Vera Cruz, Tampico, and Matamoras, along the banks of the Rio Grand del Norte, and elsewhere.

It is met with also as an endemic, although on the whole less frequently, at many points in the Sierra Templada as high as 1,200 to 1,500 metres (as in Orizaba and Oaxaca); it is only on the table-land proper (Anahuac) that it vanishes entirely, so that at the elevation of the City of Mexico malarial fever is observed only as an epidemic now and then.

On the *Pacific coast of Mexico* the circumstances as regards endemic malaria are the same as for the adjoining coast of Central America; here also the endemic fevers are confined to a few points, among which may be mentioned Acapulco, Tepic, and the strip of coast from San Blas to Mazatlan.

United States.—Beyond the Rio del Norte this great malarial region extends over the whole *Gulf coast of the United States* as far as the Cape of Florida, spreading far into the interior of the continent along the Colorado, Brazos, and Mississippi and their tributaries. In *Texas* the malarial region stretches from the coast and the swampy banks of the Rio del Norte, Nueces, Colorado, and the smaller coast streams up into the highlands, where foci of severe sickness are met with as high as the upper basin of the Colorado (Fort Duncan, in Eagle Pass), and at Fort McKavit at a height of 600 metres. The disease appears to be still more widely diffused in *New Mexico*, being met with at elevations of over 2,000 metres in Fort Bayard, Fort Union, and other places, and forming a terrible scourge to such of the native population of the country as inhabit the damp valleys. The limit of its endemic prevalence here is Santa Fé (2,300 metres), where malarial fever is no longer met with. From the western part of the *Louisiana* coast between the Sabine and the Mississippi, the malarial region extends across the zone of bluffs in that State, over a great part of *Arkansas*, particularly along the banks of the Mississippi and Arkansas rivers, and over the marshy plains in the northeast of the country, stretching away toward Missouri, and still farther along the Arkansas River over the eastern part of the *Indian Territory*, including the malarious spots of Fort Gibson (noted as the "charnel-house of the army") and Fort Sill.

Malarial disease is endemic at only a few scattered points in the great prairie land of this Territory, which rises toward the Rocky Mountains from southeast to northwest, and has a dry, sandy soil, not often saturated by any heavy falls of rain. In like manner the eastern part of Louisiana beyond the Mississippi forms part of a region little subject to malaria. This region includes the coasts and the hilly zone of the State of *Mississippi*, and in particular the Pine Woods, so much reputed for their healthiness, a range of moderately high sand dunes, covered with fir woods, which begin at Lake Ponchartrain and run along the coast, at no great distance inland, as far as the Bay of Pensacola, intersected by the Pearl River and by the Pascagoula, Perdido, and Alabama. These Pine Woods are much resorted to by the inhabitants of New Orleans and Mobile when malarial fevers and yellow fever are prevalent.

On the belt of hills in Mississippi, as far as Vicksburg, malarial endemics are met with at isolated points only, as for instance, on Grand Gulf, which is notorious for its fever; but from Vicksburg there spreads out along the valley of the Yazoo a great swampy plain rising toward Memphis, noted for the endemic prevalence of severe malaria ("Yazoo swamp fever"). The eastern hill region of Mississippi is well situated as regards healthiness, and that is the case also with the greater part of the sparsely populated State of *Alabama*, in which malaria is endemic chiefly on the coast, especially around the swamps on the Bay of Mobile, on the banks of the Alabama and Black Warrior (counties of Wilcox, Dallas, Lowndes, Montgomery, and Tuscaloosa), and on the marshy plains of Huntsville, lying to the south of Tennessee and reaching to the borders of that State. In the peninsula of *Florida* the sickness is widely diffused on the Gulf coast with its jungles and swamps, particularly in the counties of Escambia (including Pensacola) and Gadsden, at Tampa Bay, Fort Meade, and other places. The same is true also for part of the Atlantic coast, but in a lesser degree; for the health there, especially in St. Augustine, appears to have improved materially in recent years. But the chief seat of malaria in this State is formed by the plains of the interior, partly swamp, and also by the plateau of no great elevation which forms the water-shed for the Bay of Tampa and runs up the peninsula to Georgia. In *Georgia* the disease prevails widely and in severe forms, not only in the numerous creeks of the coast, but also in the interior, the neglect of agriculture in quite recent times having greatly conduced, as it seems, to an increase both in the amount and intensity of endemic fever.

In the central States of the Union malaria is endemic to an extent that is still considerable, though materially less than in the Southern States, and chiefly on the coasts of *South Carolina*, *North Carolina*, *Virginia*, and *Maryland*, and on the damp river banks of the interior. Improvement of the soil has helped not a little to narrow the range of the endemic in these States, but it is rather remarkable that malarial fevers have increased within the last twenty years in localities formerly little touched by them, especially in the mountainous districts of Virginia. In the inland central States of *Tennessee* and *Kentucky* malarial fever occurs to a moderate extent along the banks of the Mississippi and Ohio, attaining its greatest prevalence on the prairies of the latter State known as "The Barrens." On the prairie States proper—*Ohio*, *Indiana*, *Illinois*, *Minnesota*, *Wisconsin*, and *Michigan*—malarial fevers are likewise widely prevalent, diminishing in frequency, however, toward the northwest. Thus in the northern parts of Iowa the fever is no longer so common as in lower latitudes under the same circumstances of tillage; and that is the case also in Wisconsin and Minnesota, where the rate of sickness among the troops (in Fort Snelling, 42.52° N., and in Fort Ripley, 46.10° N., both on the Mississippi) amounts to about fifteen per cent. only; still more is it the case in the Territories of Dakota and Montana, where the rate falls respectively to five per cent. and six per cent. The largest foci of disease in those regions are met with on the shores of the great lakes; and here, again, the geographical situation proves to have the most decided influence on the occurrence of malarial sickness. Thus the shores of Lake Superior, and in part also those of Lake Michigan and Lake Huron, are entirely free from fever; it is not endemic, for example, at Winnebago, Wis., in latitude 44° N., notwithstanding marshes and a damp river bank, and it is comparatively rare in the swampy settlement of Fort Brady. It is in the southern parts of the State of Michigan that we come upon the true domain of malaria, and we then follow it along both shores of Lake St. Clair to the junction with Lake Huron, and along the southern shores of Lake Erie and Lake Ontario as far as the St. Lawrence. Detailed accounts from that region speak of pernicious malarial fevers at Fort Gratiot, Detroit, Plymouth, and other places on the United States side, and at Amherstbury, Fort Malden, Sandwich, etc., on the Canadian side. Even on the northern side the range of sickness on Lake Ontario extends from Hamilton to Kingston, and still farther up the ridge which runs along the shore from Burlington to the mouth of the Trent, attaining in some places a height of more than six hundred feet.

These lake-shore endemics of fever extend also to the northwestern parts of the State of *New York*, although there are many localities in the counties of Onondaga, Tompkins, Seneca, Oneida, Ontario, and others, formerly much subject to fever, that have now become tolerably free from it owing to improvements in the soil. It is mostly along the banks of the Hudson and on a narrow strip of the coast that the sickness is endemic in this State, but within the last twenty or thirty years a remarkable increase of fever has been noted in the counties situated among the mountains. The same thing has been observed also in *Pennsylvania;* as the disease has retired from places that used to be its headquarters, such as the country bordering the Schuylkill, the Susquehanna, and the Delaware, it has come to be more prominent in the mountain districts of the State. It must remain an open question how far improvements in the soil have contributed to this decrease of malaria in its old foci; at the same time it is undoubted that it has been observed to disappear from localities where no changes in the ground have taken place. The latter circumstance obtains, in part at least, for *New Jersey* also, where there has been a remarkable decrease of malarial fevers within recent years in many localities that used to be visited by it severely.

In the *New England States* malarial fever is endemic at only a few points; in the State of Maine it is no longer endemic.[1]

Neither is it endemic throughout the greater part of British North America. For *Canada*, as well as the whole inland basin of the continent, Kingston (44.8° N.) is the northern limit of endemic malaria. As an epidemic one meets it at higher latitudes on the banks of the St. Lawrence and its tributaries, on Lake St. Peter, very rarely at Montreal or Quebec, or places on the coast, such as Halifax (N. S.) and Miquelon (N. F.), in the latitude of 46.30° N. The cases in *Nova Scotia* and *New Brunswick* are imported ones. In *Greenland* malarial fever is quite unknown.

In the western regions of North America the limit of malaria reaches to somewhat higher latitudes. It is prevalent there chiefly on the slopes and in the valleys of the Rocky Mountains—whence the name of "mountain fever"—in the Territories of Wyoming, Utah, and Colorado, and it is especially disastrous to the Indian tribes. Only imported cases occur at Fort Vancouver (*Washington Territory*), in latitude 45.40° N., and on the *Oregon* coast, as well as in *Alaska*. Not until *California* do we reach a more considerable malarial region on the west coast; it extends up the valleys of the Sacramento and San Joaquin, and in the inland southern part of the State (Arizona) malarial fevers appear to be widely prevalent. But the sub-tropical coast of Southern California, from Monterey to San Diego, enjoys a noteworthy immunity from the sickness, being in that respect similarly situated with the Pacific coast of Mexico and Central America.

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[1] The reappearance of malaria in New England, and especially in Connecticut, is referred to as follows on another page:

"This reappearance of malarial fever dates from the year 1866. New Haven was the centre, and in the years following, down to 1872, the disease spread all round to Fair Haven, East Haven, Bradford, Guilford, North Haven, Hamden, and Meriden. Several observers in Connecticut have pointed out that the disease showed itself and got diffused coincidently with the making of railway cuttings, the excavation of canals, and such like earthworks; but we take it that these are not the only circumstances in which the essential cause is to be sought, for the reason that malarial fever has subsequently shown itself in localities where that etiological factor is not available, and further, by reason of the fact, which many practitioners vouch for, that numerous other forms of disease have assumed a character peculiar to and typical of malarial sickness, and have proved much more amenable to treatment by quinine than formerly" (op. cit., p. 232).

EPIDEMICS AND PANDEMICS.

The area of distribution of malarial disease here sketched in general outlines will have to be considerably extended if we take into account not merely the endemic occurrence of the sickness, as we have hitherto done, but also those regions in which the disease appears only now and then as an epidemic. These *epidemics of malaria*, which extend not unfrequently over large tracts of country, and sometimes even over whole divisions of the globe, forming true *pandemics*, correspond always in time with a considerable increase in the amount of sickness at the endemic malarious foci, whether near or distant; they either die out after lasting a few months, or they continue—and this applies particularly to the great pandemic outbreaks—for several years, with regular fluctuations depending on seasonal influences.

On the very verge of the period to which the history of malarial epidemics can be traced back, we meet with a pandemic of that sort, in the years 1557 and 1558, which is said to have overrun all Europe. It is impossible to decide, from the scanty and incomplete epidemiological data of the sixteenth and seventeenth centuries, how often such epidemic outbreaks of malarial fever may have recurred in times subsequent to that pandemic. It is not until the years 1678–1682 that we again meet with definite facts relating to an epidemic extending over a great part of Europe, and thereafter follow at short intervals reports of the same kind for the years 1718–1722, 1748–1750, 1770–1772, and for a more restricted epidemic in 1779–1783. Although malarial fever during the last ten years of the previous century and the first five years of the present had absolutely disappeared from the arena of national pestilences, and had even diminished considerably in those places where it was endemic, there developed in 1806 a pandemic of malaria which overran a large part of the north and northeast of Europe, lasting till 1812. It coincided with an epidemic of malaria in Southern India in 1809–1811, which extended from the slopes of the Mysore Mountains to Cape Comorin, and from the Western Ghâts to the Coromandel coast. During the ten years following malarial fever was again confined within its habitual limits; but thereafter, a little earlier or a little later in the same regions, there arose one of the most extensive, severe, and persistent of pandemics, beginning in 1823 and dying out in 1827, of which there are numerous medical reports from almost all parts of the world. The next general epidemic prevalence of malarial fever falls in the years 1845–1849, after which comes the great pandemic of 1855–1860. Finally, we have the malarial pestilence of 1866–1872, in which the disease spread not only over a great part of Europe, but visited simultaneously many parts of India (Presidency of Madras, Lower Bengal, Punjaub, etc.) and of North America, and showed itself for the first time, and that too in a severe form, in the islands of Mauritius and Réunion.

Decrease or Disappearance.—To complete this account of the historical and geographical aspects of malarial disease, we must first of all observe that in many parts of Europe and North America it has become of recent years not only less frequent than in the previous century, but also less severe in type. Pernicious malarial fever was prevalent as late as the eighteenth century in many parts of Germany, in the Hartz, in Augsburg, Saxony, Silesia, Würtemburg, and other localities where now it occurs only in occasional epidemics, and then always in its mildest forms. At the time of Sydenham and Willis and of Huxham, London and Plymouth were dangerous fever spots, whereas to-day malaria is a rare thing in them; and the same applies to Stourport, Bolton, and other towns in England. In Scotland, where there were still many endemic malarial foci remaining in the eighteenth century, the disease is now extremely rare. It is the same in Ireland, where, as Wylde remarks, no acute infective disease is so rarely met with as malarial fever. It is further noteworthy that the disease has become less common and milder in character in the Netherlands, in many parts of Belgium, and at numerous points in the United States of America, particularly in certain counties of Pennsylvania, New York, New Jersey, and Maryland, that used to be subject to fever; in some of the Southern States also, such as Florida, the disease has assumed a decidedly milder form.

Fluctuations.—Not less striking than this gradual subsidence and disappearance of the disease are the fluctuations observed, at several places, in the amount of the sickness, partly connected no doubt with the already-mentioned pandemic outbreaks of malaria, but to some extent independent of these. Another noteworthy circumstance is the development of endemic foci of malaria at places that had been hitherto quite exempt, or only occasionally visited by epidemics.

Thus, to mention only a few of the facts, a wide-spread outbreak of malarial fever appeared in 1823 at Prague, where the disease had not been known for years ; it continued until 1830, when it again became very rare, and it did not receive any considerable fresh accession until 1846. At Stuttgart, where malarial fevers are counted among the diseases most rarely observed, the sickness, after being epidemic in 1826, and having been completely extinguished, broke out still more extensively in 1834, and showed itself in the very same year at other places in Würtemburg occupying elevated and dry situations. At Königsburg (province of Prussia), where the conditions of the soil are very favorable to malaria, the sickness was scarcely observed at all from 1811 to 1825, but after that an epidemic of it developed which lasted until 1833 ; from 1833 to 1841 the disease recurred in isolated cases only ; from 1841 to 1852 it appeared every year in the spring to a moderate extent, but from 1852 to 1855 it was prevalent to an extent and of a severity that one but rarely sees in so high a latitude. Observations to the same or corresponding effect have been made at Marienwerder, Leipzig, Erlangen, and other places in Europe ; also in the more intense centres of malaria, as many facts from tropical countries prove.

New Foci.—A phenomenon not less interesting meets us in the fact, often observed in more recent times, of new foci of malaria being established, or of its epidemic continuance for several years, and its wide diffusion, in localities which had previously been quite free from it, or at least practically free from it.

One of the islands of the Indian Archipelago, Amboina, had, until the year 1835, enjoyed a remarkable immunity from malarial sickness, but in that year a severe epidemic arose, it is said in consequence of an earthquake that took place at the time, and since then the island has been a permanent seat of pernicious malarial fever, and has consequently become one of the most unhealthy places in the East Indies. The East African islands of Mauritius and Réunion experienced the same fate in 1866 ; they had previously been almost exempt from malarial fever, but in that year the disastrous malarial epidemic developed, and its persistence to the present time makes it probable that endemic foci of the disease have been established. In Chili, where malarial fever was formerly almost unknown, the disease showed itself in 1851 as an epidemic, and it now appears to have become domiciled at several places in that country.

While in the interest of our readers we have availed ourselves thus freely of the literary researches of Hirsch, we are not prepared to accept his account of epidemics and pandemics of malarial fevers as relating in all cases to fevers corresponding in their etiology with our endemic periodic fevers. The older writers used the word malarial in the broadest sense, and even at the present day many practitioners in the yellow-fever zone—especially in the West Indies—consider this disease as nothing more than a severe manifestation of the malarial poison. Other forms of continued fever, which we are not willing to admit into the category of malarial diseases, are also denominated "malarial" by many practitioners in various parts of the world ; and in India it is only very recently that the English physicians have come to recognize the fact that enteric fever prevails extensively side by side with malarial fevers, with which it was formerly confounded. As examples of epidemics pronounced malarial, but in which we suspect a different etiology, we may refer to the epidemic in 1835 on the island of Amboina, and to that of 1866 which invaded the East African islands of Réunion and Mauritius. We are informed with reference to Amboina that a "*pernicious* malarial fever" has taken possession of this previously healthy island since the "severe epidemic" of 1866, and we cannot avoid the suspicion that this pernicious malarial fever is essentially different from the endemic intermittent and remittent fevers of our own country, although we have no clinical data upon which to found such a suspicion. In the case of the epidemic which in 1866 visited the island of Mauritius, we have, however, fuller information. The French author Pellerean informs us that endemic malarial fevers of a comparatively mild type prevailed upon this island long prior to the "disastrous epidemic" of 1866. Hirsch's supposition, therefore, that endemic foci were established as a result of this epidemic is not required to explain the facts relating to the endemic prevalence of malaria, and, as we have pointed out on another page (page 17), the history of this violent epidemic, the evidence relating to the transportation of the disease to distant localities, and the clinical features as given by observers on the spot—who, however, pronounced the disease malarial—force upon us the conviction that the malaria which was the cause of this epidemic outbreak must have been essentially different from that widely distributed telluric poison which is concerned in the etiology of endemic periodic fevers.

PART SECOND.

MALARIAL DISEASES.

CHAPTER VIII.

MALARIAL INTERMITTENT FEVER.

DEFINITION.—A periodic fever of malarial origin, in which a series of paroxysms occurs at definite intervals, and in which there is a complete intermission of the febrile phenomena between these paroxysms. The febrile attack is commonly ushered in by a distinct chill and terminates in copious perspiration.

SYNONYMS.—Febris Intermittens, Fever and Ague, Periodic Fever, Paludal Fever, Ague.

Inasmuch as intermittent febrile phenomena may be produced by other toxic agents—*e.g.*, the septic poison, morphia—it has been thought best to place at the head of this article the term "Malarial Intermittent Fever." Most authors, however, speak of the malarial fevers under consideration simply as "intermittent fever," and this term is so generally recognized as applying especially to periodic fevers of malarial origin, that the omission of the word *malarial* would not be likely to lead to any misapprehension.

ETIOLOGY.—Malarial intermittent fevers are directly or remotely due to the action of an unknown poison of telluric origin, called *malaria*. The effects of this poison are manifested mainly upon the nervous system; upon the blood, which is impoverished by the abundant destruction of its colored elements—red blood-globules; and upon the spleen, which is engorged during a paroxysm, and becomes much enlarged in those subject to chronic malarial poisoning.

PREDISPOSING CAUSES.—Natives of northern non-malarial regions are more susceptible to malaria than those born in the tropics, who enjoy a certain immunity, which is especially well-marked in the negro race. Aside from individual and race peculiarities, the most potent predisposing causes are debility from disease, wounds, hemorrhage, dissipation, inanition, or fatigue, and especially from previous attacks of malarial fever.

SECONDARY CAUSES.—The periodic febrile attacks which constitute "intermittent fever" may be induced by secondary causes long after the individual subject to them has removed from the locality where he was exposed to the primary cause—malaria. And, on the other hand, in malarial regions, and especially in the tropics, where diurnal variations in temperature are very slight, intense malarial poisoning may occur, as manifested by anæmia and enlargement of the spleen, without the development of intermittent fever.

The most active secondary causes are exposure of the surface of the body to chill, exposure to the heat of the sun, a cold bath, excessive exertion, mental excitement, "even a dose of purgative medicine may give rise to a paroxysm" (Wood).

The development of intermittent fever as a result of excessive diurnal changes in the external temperature has been noted by numerous observers, and some authors (Oldham, Moore, and others) have contended that the periodical refrigeration of the body due to these changes is sufficient by itself to account for the phenomena of intermittent fever. The insufficiency of this explanation has already been referred to (page 30). But that this is a potent exciting cause is beyond question, and the unusual prevalence of intermittent fevers in the autumn is no doubt partly due to this cause, which, however, has no effect except upon those who have been exposed to malarial emanations.

Fayrer says that in India, attacks of intermittent fever are very likely to occur when the diurnal changes of temperature are great; *i.e.*, at the commencement of the cold and during the drying-up season. The same author remarks: "Two of the severest attacks of ague I have had as reminiscences of remittent of former years were caused by getting into bed with cold linen sheets, and by a douche of cold water after the manipulations of the hair-cutter."[1]

INCUBATION.—The variable interval which elapses between the time of exposure and the development of a primary attack of intermittent fever is commonly spoken of as the period of incubation. But aside from the fact that we have no proof that the malarial poison incubates and multiplies within the body as does the poison of those diseases which are directly or indirectly communicable from individual to individual—*e.g.*, scarlet fever (directly communicable), typhoid fever (indirectly communicable)—there are objections to the use of this term. This period may vary from a few hours to several months; and, as already pointed out, the characteristic intermittent paroxysms are often directly due to the action of secondary causes, which may be of the most trifling nature. In these cases, at least, we must look upon the febrile paroxysm rather as an accident or sequela, depending upon former exposure to malaria, but not immediately caused by the presence of this agent in the system.

On the other hand, the primary attack may occur so promptly after exposure that there is practically no period of incubation, the vital powers being, as it were, overwhelmed at once by the intensity of the poison. As an example of this we may cite the case recorded by Professor Maclean.[2]

> The late Lieutenant-General Sir Mark Cubbon informed me that many years ago, when on a journey to the Neilgherry Hills, he was compelled to pass a night at the foot of the Segoor Pass, then an uncleared and unhealthy spot. A party of three German missionaries was also detained at the same place, and slept in the same house. These gentlemen were fresh from Europe and in high health. On the following morning they pursued their journey, and were soon "above fever range." In less than twenty-four hours three out of four of the party were stricken with fever, and two of them died in a few days.

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[1] Op. cit., p. 56.

[2] Reynolds' System of Medicine, vol. i., p. 54.

Hertz[1] says that the period of incubation is commonly reckoned at from six to twenty days, but agrees with other authors in the statement that the disease may appear immediately after the reception of the injurious influence. Among other examples of prolonged incubation given by this author the following is especially valuable. The case is reported by Bioxall.

A man-of-war spent five days in the harbor of Port Louis. As a result of exposure at this place, two of her crew were attacked with quotidian intermittent fever at the end of twelve and of fourteen days, and two others with tertian fever at the end, respectively, of forty-eight and one hundred and eighty-four days after embarkation.

Fayrer has known more than one case where the first paroxysm of ague has occurred more than a month after exposure, but says that "simple ague generally occurs earlier, in a few days or even hours."[2]

TYPES.—The paroxysms of malarial intermittent fever usually occur with great regularity at intervals of twenty-four, forty-eight, or seventy-two hours, and the three principal types of the disease receive their names from this circumstance, viz.: the *quotidian*, characterized by a daily paroxysm; the *tertian*, characterized by a paroxysm every second day; the *quartan*, in which the paroxysm occurs every third day.

"The inventors of the two latter names considered the two nearest paroxysmal days with the intervening day or days as constituting one period, and thus counted every paroxysmal day twice in succession" (Wood[3]).

Authors have also mentioned types having a more prolonged period of intermission, *quintan*, *sextan*, *septan*, and *octan*; but if cases occur which are properly referred to these types they are so rare that few practitioners have had the opportunity to observe them.

The common types present several varieties which have received special names. Thus we may have a *double quotidian* (int. quotidiana duplicata), in which two daily paroxysms, often differing in intensity, occur at different times during the day. Or a daily paroxysm may occur which is not uniform as to character and the hour of its return, but which will be found to make up two rhythmical series, the paroxysms of each alternate day corresponding with each other. A fever presenting these characters is of the tertian type, notwithstanding the fact that there is a daily paroxysm, for the attacks of the first and third day being alike, and those of the second and fourth day apparently constituting an independent series, the fever is considered a *double tertian*.

Again, there may be two paroxysms one day and none the next—called *duplicated* or *doubled tertian*; or two paroxysms on one day and one the following day—*triple tertian*. Authors also refer to a *double quartan* in which paroxysms occur, at different hours, two days in succession, while the third day is passed without an attack; and *triple quartans* in which there is a daily paroxysm, but in which the paroxysms on three successive days differ from each other, while each makes up a rhythmical series when considered in connection with other paroxysms occurring at intervals of seventy-two hours. Still other varieties have been mentioned as the *tripled* and *quadrupled tertian*, the *doubled* and *tripled quartan*, the combination of a quotidian and tertian, etc. Finally, persons who have suffered repeatedly from intermittent fever may have attacks which seem to follow no regular rule of return, and which have been designated *erratic intermittent*.

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[1] Ziemssen, vol. ii., p. 588.

[2] Op. cit., p. 78.

[3] Practice of Medicine, vol. i., p. 254.

According to Hertz, the double types seldom appear as such primarily, but arise in the course of a prolonged attack or in the relapses which occur long after exposure. The rhythm—type—of an intermittent fever may be changed by the recurrence of the paroxysms at intervals greater or less than twenty-four hours, or a multiple thereof. Thus by the interval being gradually prolonged a quotidian may be transformed into a tertian; or, on the other hand, by *anticipating*, a quartan may be changed into a tertian, a tertian into a quotidian, or a quotidian may assume a remittent form.

It is evident that these different types depend upon peculiarities relating to the individual and not upon the nature of the poison to which they are directly or remotely due. This is shown by the fact that exposure under identical circumstances may in one person produce a quotidian and in another a tertian intermittent; and also by the fact that attacks in the same individual, after removal from the locality where exposure occurred, may exhibit different types of periodicity. This gives support to the view that these paroxysms are of neurotic origin.

The tendency of intermittent paroxysms to recur at definite intervals is further shown by the relapses which occur so frequently after the patient has apparently been cured by the administration of quinine. These relapses are especially liable to occur at the end of seven or fourteen days from the date of the last paroxysm. The quartan type is said to be peculiarly subject to these relapses, which occur often at the end of a month on the exact day which would have been the "fever-day" if there had been no interruption in the course of the disease.

First attacks are usually quotidian, especially in the tropics, and in temperate latitudes during an unusually hot summer (Hertz). The paroxysms in this type are more prolonged than in the tertian and quartan, and the intermission is often so brief or ill-defined that the fever becomes virtually a remittent. Hertz says: "When successive paroxysms follow one another so rapidly that the chill of the second occurs in the sweating stage of the first we designate it as *febris subintrans*, and it constitutes a transition stage to the remittent and sub-continued type of fevers."[1]

In temperate climates the tertian is the type which occurs most frequently, and some authors have considered this the primary type of intermittent fever. This certainly is not true as a general rule, although it is no doubt the primary and only type observed in many cases occurring in the northern portions of the United States and in temperate regions generally.

The quartan type is said to be almost unknown in tropical regions. In India and China a first attack of ague invariably takes the quotidian form (Maclean).

"Quotidian ague is apparently the type in first attacks in India. Tertian occurs more frequently in those who have suffered previously, and in whom alterations of temperature, fatigue, irregularities of living, and so on, have re-excited it—being evidence not of recent but of pre-existing disease. According to Morehead, quotidian prevails in the rainy season of the southwest monsoon from May to October. Tertians are met with in the cold season, as the result of alteration of temperature, in those who have resided long in malarious localities, and are frequently complicated with enlarged spleen.

Tertian seems to be most common in Europe, then quartan, and last quotidian. In Africa, the West Indies, and India, the quotidian is most frequent. In Burmah, according to Murchison, 83.5 per cent. were quotidian, and 1.6 per cent. tertian. In India, according to Waring, the observations of several medical officers in various stations throughout India and the Tenasserim provinces show that of 2,574 cases of ague 1,822 were quotidian, 595 were tertian, 29 quartan, 118 double tertian, 10 irregular; and he further states that of 53,753 admissions of European troops, 51,287 were quotidian with 646 deaths, 2,097 tertians with 12 deaths, 2,369 quartans with 2 deaths. Dr. Burton Brown says: "At least 95 per cent. of our cases of fever at Lahore are intermittent quotidian agues, about 3 per cent. tertians, and the rest quartan ague, remittent fever, *and enteric fever.*"[1]

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[1] Ziemssen, vol. ii., p. 594.

Dr. Morehead says:

> It has been generally stated by systematic writers, that of the three leading forms, the tertian is the most frequent, then the quotidian, and lastly the quartan.
>
> The statement relative to the quartan type will be generally accepted. Of 243 cases of intermittent fever in natives of different castes in Bombay, selected for the purpose of clinical instruction, there was not a single instance of the quartan form. Of 1,344 cases of intermittent fever treated during the period of my service in the European General Hospital, the quartans, if any, were very few in number.
>
> That tertians are more common than quotidians is not confirmed by my experience, and is opposed to that of observers in India generally. Of the 243 clinical cases, 211 were quotidians and 27 tertians, and of 5 the type has not been recorded. . . .
>
> Quotidians will be found to prevail most generally at those seasons of the year when the generation of malaria is supposed to be actively going on; and they may probably be viewed as affording evidence of the recent action of the morbific cause. It is the type which the disease for the most part assumes in first attacks. Tertians, on the other hand, usually occur in individuals who have suffered on previous occasions, and in whom the fresh attack is often traceable to ordinary and recently applied exciting causes, as sudden alterations of temperature, atmospheric moisture, fatigue, debauch, etc. The occurrence of this type may generally be regarded, not as the evidence of the recent introduction of malaria into the system, but as that of a pre-existing, abiding influence, some time dormant, now re-excited into action by an ordinary cause.[2]

Boudin[3] would attribute the difference in the type of the malarial fevers entirely to difference in intensity of the morbific agent, and points to the fact that quartans are most common near the northern limit of prevalence; that tertians are the prevailing type in temperate latitudes, and that as we approach the equator the type more nearly approaches the continued form, the fevers in the tropics being quotidian, remittent, or continued.

Colin opposes this view, and ascribes the difference in type mainly to the difference in temperature and to the date of "intoxication." He says:

> We cannot admit that there is a correlation between the intensity of intoxication and the type of the morbid phenomena, this approaching the continued form according as the degree of intoxication is greater, while with a smaller dose the intoxication produces morbid accidents more distant, more intermittent. We shall see, on the contrary, that in hot countries the most continued forms generally manifest themselves before the emanations from the soil have reached their maximum of intensity. On the other hand, they are most common among the new-comers, while the tertian, quartan, "*septénaire*," and others still more rare are found in individuals previously attacked and profoundly intoxicated.
>
> It is then far less the intensity of action of the miasm than these two influences of a different order—temperature and date of intoxication—which controls the type, be it continued or intermittent.
>
> The influence of temperature is shown first by the geographical distribution of the different forms, which are the more continued as we observe them nearer the equator, the more intermittent as we observe them near their northern limit. This is a fact which is established by observations collected in all parts of the world. Thus in the

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[1] Fayrer, op. cit., p. 66.

[2] Researches on Disease in India, p. 17.

[3] Traité des fièvres intermittentes. Paris, 1842.

centre of Europe the tertian type is the most frequent. Griesinger has seen at Tübingen 268 tertians to 122 quotidians, and most of the German observers have noted analogous proportions. In these regions the attempt has been made to show that the tertian is the fundamental type, the first rhythm of intermittent fever. As we go southward we observe not only the augmentation of the quotidians, but also of the remittents. . . . This transition is especially marked in Algeria, where the remittent types are more frequent, at the same time that among the periodic fevers the type—quotidian—in which the attacks are the nearest together is the predominant form. Finally, in the tropics the intermittents of all types, even the quotidians, are relatively rare as compared with continued types.

Table No. III. will complete the demonstration of this distribution of fevers according to their type. In it are brought together the statistics from three very different latitudes, and the law of geographical distribution is admirably shown.

	Total number of cases.	Remittent, per cent.	Quotidian, per cent.	Tertian, per cent.	Quartan, per cent.	Irregular, per cent.
Vienna[1].....................	3,125	....	36	42	7.6	3
Algeria[2].....................	4,849	12	62	24	0.5	...
India[3]......................	5,617	91	7	1	....	....

The influence of heat upon the type is shown, in the second place, by the intimate relation of the various forms with the seasons. In Rome we only encounter, in the most absolute manner, remittents and continued forms during the hottest season—during the month of July and the first half of August—when they alone constitute almost the entire epidemic. The quotidians, and then the tertians, do not become frequent until the end of August, equalling then only the number of remittents, which disappear during the month of September and leave the periodic types to occupy the ground. Among these the last to appear is the quartan type, which is extremely rare before the end of September, becomes more common in October, and sometimes equals in November the other types, which are less compatible with the lower temperature. . . .

It remains for us to study the influence of the date of infection of the person attacked upon the type of the febrile manifestation. This question seems to us one of extreme importance. It is from neglecting to consider it that no explanation has heretofore been given of the fact that, in the same surroundings, certain individuals are attacked with periodic fevers and others with continued fevers, and why in different localities one type predominates rather than another; a fact which has caused eminent clinicians—Trousseau for example—to suppose that there may be special centres (*foyers*) for each of these types.

We can formulate at the outset the following propositions: In general, the more an individual is poisoned by malaria and subject consequently to relapses, the greater will be the predisposition to the types having paroxysms at prolonged intervals. On the contrary, the greater his previous immunity the greater will be the tendency to types having a brief intermission and to the continued form. Thus in our army at Rome, those who had recently arrived were attacked with continued, remittent, or quotidian fever, while the old soldiers were attacked with tertian or quartan fevers.

We beg the reader not to suppose that we claim that there is an absolute and systematic succession in these different manifestations of malarial poisoning. We see constantly the different types succeed each other in the same subject without the least appearance of conformity to the law we have formulated—thus the quotidian may replace the tertian; but nevertheless, our proposition is in a general way perfectly true, although it only becomes evident by the comparison of a considerable number of cases belonging to different categories. In Rome we were able to compare the cases among the French soldiers, among whom the exposure was comparatively recent, dating from a few months to a few years, with those among the adult civil population exposed from birth. The records of our military hospitals show that our soldiers afforded about the same number of tertians as of quotidians, whereas there were ten times as many tertians as quotidians among the adult natives admitted to the civil hospital of San Spirito.[1]

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[1] Annual Reports of the General Hospital of Vienna for the years 1855–62 (Griesinger).

[2] Finot: Compte rendu du service médical de l'hopital militaire de Blidah, pendant l'anne 1842 (Recueil des mém. de méd. militaire, t. lvi.).

[3] Martin: Statistics of the General Hospital of the Presidency of Bengal for twelve years (The Influence of Tropical Climate, p. 55).

The relative proportion of the different types of intermittent fever in our armies during the late war is given in the following table:[2]

	White Troops.		Colored Troops.	
	Cases.	Per cent.	Cases.	Per cent.
Quotidian	447,258	51.77	63,992	53.79
Tertian	375,170	43.44	51,045	42.91
Quartan	41,223	4.78	3,923	3.29

The following table[3] represents the total number of cases of intermittent fever in the army of the United States for eighteen years prior to the civil war (from 1840 to 1859, excluding the two years of the Mexican war—1847–48):

	No. of cases.	Per cent.
Quotidian intermittent	51,623	52.6
Tertian intermittent	44,857	45.6
Quartan intermittent	1,757	1.8

SIMPLE INTERMITTENT FEVER.

In simple intermittent fever a well-defined febrile paroxysm, usually ushered in by a chill and terminating in perspiration, occurs at definite intervals. During the *intermission* between two such paroxysms the patient remains free from fever and is commonly able to pursue his ordinary occupation, especially when the fever is of the tertian or quartan type. There is often, however, during the period of apyrexia a certain degree of debility, and in some cases more or less gastric disturbance, loss of appetite, and irregularity of the bowels. The patient may complain of feeling tired, his strength is exhausted by slight exertion, he is irritable and nervous, has occasional attacks of frontal headache, pains in his limbs, etc. All of these symptoms are more marked in the apyretic stage of a primary attack, which, as we have just seen, is commonly of the quotidian type. The period of pyrexia is more prolonged in this type, and the intermission may be so brief that the fever approaches the remittent in character. In this case there is no time during the twenty-four hours when the patient feels entirely well. His secretions generally are disordered, the tongue coated, the urine scanty and high-colored, the pulse frequent, and the nervous symptoms more or less distressing. On the other hand, intermissions in the more prolonged types, and especially in relapses occurring long after the primary exposure and due to secondary causes, are periods of comparative health and strength.

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[1] Colin, op. cit., pp. 135–145.

[2] From the first medical volume of the Medical and Surgical History of the War of the Rebellion.

[3] From Woodward's Camp Diseases, Philadelphia, 1833, p. 165.

DIAGNOSIS.—The dividing line between quotidian intermittent and remittent fever is not sharply drawn, and one form frequently passes into the other. When there is a period of complete apyrexia, however brief, the case should be diagnosed as intermittent. In remittent fever, on the other hand, there is merely an abatement of the febrile movement during the *remission*, and this is often found to be less in amount, as shown by the clinical thermometer, than the greatly improved feelings of the patient, his pulse, and the sensation given upon applying the hand to the surface of his body would indicate.

> It is not unusual for cases of fever, remittent at their commencement, to become intermittent before their close, or for cases that have been intermittent at the outset to pass into the remittent form in their advanced stages. Instances are also not unfrequently met with which seem to occupy an intermediate position, which by some would be classed as intermittents, by others as remittents—cases in which there is an intermission of the pyrexia, but in which the tongue continues coated, the secretions more or less deranged, and the succeeding paroxysm comes on gradually without rigor.[1]

Intermittent fever from septic poisoning and the hectic fever of phthisis are to be distinguished from malarial intermittent by the fact that the paroxysms are less regular as to the time of their recurrence, and not so well defined and abrupt in their commencement and termination. Indeed, the fever is rather remittent than intermittent in character. Moreover, in hectic fever we have the physical signs of the local disease in the lungs to which the fever is due, the night-sweats, the frequent pulse, the bright eye and clear complexion. The differential diagnosis, therefore, is not difficult. The rigors and fever of septic poisoning from absorption of poisonous products formed in the uterus, in pus-cavities or in sinuses, as a result of putrefactive decomposition, may also be traced to local lesions, and the febrile phenomena do not usually present a definitely periodic character.

PROGNOSIS.—It may be questioned whether *simple* intermittent fever is ever directly fatal, notwithstanding the fact that a certain number of deaths are recorded under this heading in our mortality statistics from various sources (see page 88). Indirectly, however, intermittent fever—or at least the malarial poison to which the intermittent phenomena are directly or remotely due—is responsible for a large number of deaths which appear under other headings. Many of the deaths from chronic visceral disease, from "dropsy," from dysentery, and from chronic diarrhœa, occur among the victims of chronic malarial poisoning. Whether an organic lesion of the heart, liver, or kidneys be a result of protracted intermittent fever or a complication quite independent of the malarial disease, there can be no question as to the unfavorable influence of the intermittent attacks upon such organic troubles.

Intermittent fever, also, by reducing the globular richness of the blood and impairing the vital resistance of the nervous system, renders its victims especially liable to attacks of the specific febrile diseases, and no doubt adds to the mortality directly due to these diseases.

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[1] Morehead, op. cit., p. 56.

The mortality, shown by the published statistics, in the United States Army for eighteen years before the late war (1840 to 1859, excluding 1847–48, the two years of the Mexican War) was 33 out of a total of 98,237 cases, being one death to every 2,976 cases.

During the first year of the civil war the recorded mortality was nearly three times greater than this (Woodward[1]). The mortality during the entire war is given on page 83.

The number of cases of intermittent fever and the mortality reported, in that portion of the Army of the United States stationed in the territory indicated, during the four years from 1870 to 1874, is given below in tabular form.[2]

From June 30, 1870, to July 1, 1874.	No. of stations.	No. of cases.	Deaths.
Military Division of the Atlantic[3]	34	4,914	..
Military Division of the South[4]	26	6,771	9
Department of Texas[5]	15	3,284	4
Department of the Missouri[6]	20	4,146	..

We learn from this table that the mortality from intermittent fever among troops stationed in the northern portions of the United States is *nil;* and that it is only in the Southern States that a death occasionally occurs, probably from congestive intermittent.[7]

With reference to the mortality in India we quote from the valuable work of Morehead:

> The mortality in India resulting directly from simple intermittent fever is not great; but it is not accurately known nor can it be determined by ordinary hospital returns. During my service in the European Hospital, the returns show a mortality of 1.33 per cent from intermittent fever. But the complicated cases are also included; and from the greater number of deaths having taken place in December, February, March, and April, it is evident that the fatal result must have arisen from the sequelæ of the disease.
>
> Though the immediate risk to life from a paroxysm of intermittent fever is slight, still the mortality to which the disease indirectly leads is very great, though not expressed in statistical tables as at present framed.
>
> Continued exposure to malaria or frequent recurrences of intermittent fever engender, as is well known, a cachectic state of the system, in which the nutritive processes of the tissues and of the blood are defective and perverted, and in which splenic, he-

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[1] Camp Diseases, p. 165.

[2] Data obtained from Circular No. 8, Surgeon-General's Office, Washington, May 1, 1875.

[3] Embracing the States of Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut, New York, New Jersey, Pennsylvania, Delaware, Maryland, Virginia, West Virginia, Ohio, Indiana, Michigan, and Wisconsin.

[4] Embracing the States of North Carolina, South Carolina, Georgia, Florida, Alabama, Kentucky, Tennessee, Louisiana, Arkansas, and Mississippi.

[5] The State of Texas and Fort Sill, Indian Territory.

[6] Embracing the States of Missouri, Kansas, and Illinois, the Territories of Colorado and New Mexico, and Fort Gibson and Camp Supply, Indian Territory.

[7] Unfortunately the different types are not given separately in the published report from which these data have been obtained. This is to be regretted, not so much with reference to this question of mortality, for there is but little doubt as regards this, but because we are unable to study the influence of latitude—temperature—upon the type of the febrile manifestations, and thus test the accuracy of the views of M. Colin.

> patic, and other local congestions tend to occur. This cachexia not infrequently terminates in death by exhaustion. But it is not in this manner that the indirect mortality from intermittent fever chiefly arises. It takes place because the cachexia caused by the fever is a state in which the system becomes very predisposed to local inflammation or congestion under the influence of external cold. The structure most liable to be thus affected is the mucous lining of the intestinal canal; and the diseases induced are classed, in the hospital returns, under the heads diarrhœa and dysentery. There can be no question that much of the mortality attributed in India to "bowel complaints" is, though indirectly, yet fairly chargeable to the account of the malarious fevers. The principal season of malarious fever, excited by the direct action of malaria, and consequently the chief season during which this deterioration of the system occurs, may, in general terms, be said to range from June to the end of November. Then follow December, January, February, and March, with their lower absolute temperature, their greater range, their frequent chilling winds; and it is in these months that the asthenic constitution is liable to suffer from dysentery and diarrhœa.[1]

SYMPTOMS AND COURSE OF THE DISEASE.—*Prodromal Stage.*—First attacks of intermittent fever are not infrequently preceded by symptoms of disturbed health, which vary greatly in intensity under different circumstances, being sometimes so slight as scarcely to attract notice, and again giving decided warning that some potent disturbing agent has been introduced into the system. Those who are subject to repeated attacks of "ague" may also be conscious of a threatening attack, and nothing is more common than to hear them say, "I fear I am going to have a chill." The prodromal stage may be inaugurated almost immediately after exposure, and may not culminate in a characteristic febrile paroxysm for several days, often a week or more. The symptoms relate mainly to the nervous and digestive systems. There is often frontal headache and pain in the back and limbs, occasional chilly sensations, and a disposition to stretch and yawn; the appetite is capricious or entirely deficient, the tongue coated, and the bowels are apt to be constipated, although there may be diarrhœa. In other cases these symptoms are more pronounced, there is marked debility, severe headache, disturbed sleep, copious perspiration, or a hot, dry skin, a foul breath and coated tongue, nausea and gastric distress, a pallid and sometimes icteric complexion, tenderness on pressure over the spleen, scanty and high-colored urine, etc.

These symptoms, occurring within a few days after exposure in an intensely malarious locality, would indicate to an experienced practitioner that an attack of malarial fever was threatened, but would not furnish the basis for a prognosis as to the type or severity of the impending attack. The administration of a few full doses of quinine will often cause all of these premonitory symptoms to disappear, and the approaching paroxysm may thus be nipped in the bud.

The prodromal symptoms mentioned may gradually assume a remittent or intermittent form, or a violent rigor followed by high fever and perspiration may announce in a definite manner the nature of the disease. In many instances a pronounced paroxysm of this nature is the first manifestation of malarial poisoning, with the exception, perhaps, of slight chilly sensations and a disposition to stretch and yawn for an hour or two before the occurrence of the chill.

The Paroxysm in simple intermittent fever consists of three stages, which pass insensibly one into the other, viz., *the cold stage, the hot stage,* and *the sweating stage.* The duration of the entire paroxysm depends to a considerable extent upon the type of the febrile manifestations, being longest in the type—quotidian—having the shortest period of apyrexia, and shortest in the type having the most prolonged intermission.

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[1] Researches on Disease in India, p. 25.

Fayrer says: "The average duration of the fit is said to be about sixteen hours in the quotidian, ten in the tertian, and six in the quartan, but these are subject to so much variation that the exact types are exceptional."[1]

It is generally stated that the paroxysm is most apt to occur in the morning in the quotidian type, about noon in the tertian, and in the afternoon in the quartan. Dr. George B. Wood says:

> It is a remarkable fact that the paroxysms seldom occur during the night. Perhaps sleep may in some way oppose a resistance to their attack. The rule is not universally, but generally true. In the vast majority of cases the time of attack is between eight in the morning and eight in the evening; and it is worthy of observation that in the anticipating and retarding cases, when the receding or advancing paroxysm reaches the period of darkness, it is apt either to be arrested in its course or to leap over the night, backward into the evening or forward into the morning. Thus the paroxysm of an anticipating tertian, occurring first at noon and recurring successively at the hours of ten, eight, and six, will, after attaining the last-mentioned hour, either continue to recur at the same or will return next time at about six or eight in the evening preceding the regular period. A retarding tertian, on the contrary, after reaching the confines of night, makes its next attack in the morning subsequent to the regular day of return (Fordyce).[2]

Dr. Wood admits the general rule that the paroxysms of quotidians most frequently occur in the morning, tertians in the middle of the day, and quartans in the afternoon, but says there are many exceptions to this rule. Thus either the quotidian or tertian may occur in the afternoon. The paroxysm of a quartan, however, very rarely occurs in the morning. "Another result of observation is that the longer the duration of the disease the later in the day are usually the returns. Hence, in old cases of intermittents the paroxysms should occur in the afternoon" (Wood).

The observations of Dr. Geddes, as reported by Waring, do not accord with the rule above given so far as the quotidians and tertians are concerned. He found that the maximum number of attacks in the quotidian type occurred between 2 P.M. and 4 P.M., and in the tertian type between 9 A.M. and 11 A.M. (Fayrer).

Morehead also has noted the hour of attack in 155 out of 243 cases in India, of which 211 were quotidian, 27 tertian, and none quartan. This was between 6 A.M. and 2 P.M. in 74, and after 2 P.M. in 81. The fact that while a large majority of the cases were quotidian, a majority of the attacks did not occur until after two o'clock in the afternoon, is opposed to the statement of systematic writers, but, as pointed out by Morehead, may be accounted for by the retarding effect of antiperiodics, which were administered promptly and doubtless in full doses.[3]

This question of the hour of predilection of the attack in the various types of intermittent fever is an important and interesting one; for as Maillot has justly said, "if we could determine the conditions in virtue of which the paroxysms occur in greater number at a given hour rather than at any other, we would have made a great step in the direction of the discovery of the law of intermittence."

The following tables, which we copy from the work of Colin, frequently referred to in the present volume, give the results of extended observations, with reference to this point, made in Algeria by MM. Maillot, Finot, and Durand:

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[1] Op. cit., p. 65. [2] Practice of Medicine, vol. i., p. 258. [3] Op. cit., p. 20.

Attacks each Hour from Midnight to Noon.

	1	2	3	4	5	6	7	8	9	10	11	12
Observations of Maillot..	26	20	29	49	55	89	150	171	249	326	212	266
Observations of Finot....	24	38	45	84	78	116	145	196	227	309	183	284
Observations of Durand..	7	22	20	18	39	57	59	124	133	172	103	164
Total................	57	80	94	151	172	262	354	491	609	807	498	714

Attacks each Hour from Noon to Midnight.

	1	2	3	4	5	6	7	8	9	10	11	12
Observations of Maillot...	103	155	80	86	67	59	29	32	8	29	17	11
Observations of Finot....	96	159	106	88	104	169	62	69	43	66	23	48
Observations of Durand...	76	98	70	65	56	83	41	52	23	26	17	20
Total................	275	412	256	239	227	311	132	153	74	121	57	79

These tables show that 1,430 attacks occurred between the hours of 6 P.M. and 6 A.M., and that nearly four times as many attacks (5,296) occurred between the hours of 6 A.M. and 6 P.M.

The number of attacks during the morning hours, 6 A.M. to 12 M., was 3,474, which is about twice as large a number as occurred in the afternoon, from 12 M. to 6 P.M., viz., 1,820.

The statement made by Wood and others, that in the tertian type the attacks commonly occur in the afternoon, is not opposed by those observations which, no doubt, relate mainly to the quotidian type, which in the latitude of Algeria is by far the most frequent.

Cold Stage.—The cold stage of an intermittent fever is commonly ushered in by a feeling of general discomfort and disposition to yawn and stretch the limbs; the patient complains of feeling dizzy, or his head aches, or he may be simply sleepy and indisposed to exertion; often he has pains in the limbs and back, and at the outset slight chilly sensations along the spine and extending over the surface of the body. The chill may amount to nothing more than this, and may quickly give place to the hot stage, which, indeed, has already commenced so far as an actual rise of temperature is concerned. But very commonly the rigor is more pronounced and is attended with chattering of the teeth, convulsive shuddering of the body, a pallid appearance of the surface, a pinched nose, livid or pallid lips, and sunken eyes; the extremities are cold and shrivelled in appearance, and the blue color of the nails indicates the sluggish arterial circulation, which is further shown by the small and rapid pulse or by a feeble and irregular action of the heart. The skin often presents the rough appearance known popularly as "goose-flesh," and the surface of the body feels cool to the touch and is deficient in sensibility. The respiration is commonly somewhat accelerated and sighing in character, and the patient may complain of a feeling of constriction across the chest. There may also be epigastric distress attended with nausea and vomiting or attempts to vomit. The patient frequently feels faint and has palpitation of the heart. The eyes are dull and the pupils dilated. There is apt to be thirst, although the tongue is moist and pale. The urinary secretion is copious and the urine commonly limpid and light-colored.

The congestion of internal organs which results from this determination of the blood from the surface to the interior of the body is shown by the symptoms already mentioned—drowsiness, headache, etc., from congestion of the brain; retching and bilious vomiting from congestion of the stomach and liver; præcordial oppression and hurried respiration from an overburdened heart and congestion of the lungs. The mucous membrane of the intestine may also be unduly congested, and as a result there may be copious intestinal discharges.

The duration of the cold stage may vary from a few minutes to several hours. On the average it may be stated at about an hour (Wood).

Dr. Impey (quoted by Waring) found that the average duration of the cold stage in 108 cases was one hour and twenty-five minutes. . . . In three cases there was no cold stage at all, in two it lasted ten minutes, in three not more than fifteen minutes, and in nine about half an hour. The longest duration of the cold stage was nine hours.[1]

According to Aitken, the duration of the cold stage is from a few minutes to five or six hours, and in general, if the case be severe, the shorter the cold stage the longer the hot stage. . . . The rule is that the quotidian has the shortest cold stage and the longest hot stage; the tertian a longer cold stage and a shorter hot stage than the quotidian; while the quartan has the longest cold stage and the shortest hot stage of all the varieties.[2]

While the temperature of the surface is sensibly cooler during the rigor, and the extremities may even feel cold to the touch, the temperature of the body, as shown by a thermometer under the tongue or in the axilla, commences to rise even before the patient is conscious of the approaching paroxysm. Thus Ringer has noted a rise in temperature from forty-five to ninety minutes in advance of the chill, and a continued rise during the whole of the cold stage.[3]

The fact that the temperature of the interior of the body is above the normal during the cold stage is also verified by Hertz, by Colin, and by Fayrer. The last-named author says: "The temperature begins to rise before the chilly sensation comes on, and attains its maximum, which may be from 105° to 106°, toward the end of the hot stage."

Hot Stage.—The cold stage passes gradually into the hot as the circulation becomes re-established in the periphery of the body. The tremors and chattering of the teeth give place to occasional chilly sensations and a feeling of agreeable warmth. The blanched surface resumes its natural color; the livid lips and finger-nails become red; and soon the face becomes flushed and the eyes congested. The extremities no longer feel cold to the touch, and after a time the whole surface of the body feels hot and dry. The pulse is frequent, full, and hard, the carotids throb, the mouth and lips become dry and hot, and the patient complains of unquenchable thirst. The nervous pains and præcordial uneasiness are relieved, and the respiration becomes rapid and noisy, instead of being oppressed and sighing as in the cold stage. The burning heat of the surface, increased headache, and general feeling of discomfort cause the patient to be restless and excited, and he may become delirious. The urinary secretion becomes diminished and the small amount of urine voided is of high specific gravity and dark-colored.

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[1] Fayrer, op. cit., p. 79.

[2] Science and Practice of Medicine, vol. i., p. 484.

[3] London Lancet, Aug. 6, 1859.

The intensity of the symptoms—excited circulation, headache, heat of surface, restlessness, delirium—is greater in the quotidian than in the tertian type, and in young and full-blooded persons suffering a first attack than in the cachectic victims of chronic malarial poisoning.

An erythematous or petechial eruption occasionally appears and disappears with the fever (Wood).

The duration of the hot stage varies greatly with the type of the fever, and also in cases of the same type. It may last but an hour or two, or may be extended to twelve or sixteen hours in the quotidian type; or, as already stated, the paroxysm may be so prolonged that a quotidian intermittent is changed into the remittent form.

Sweating Stage.—The stage of pyrexia terminates in a more or less profuse perspiration, during which the temperature rapidly falls to the normal, the headache, thirst, and general discomfort are relieved, and the patient often falls into a quiet sleep. Perspiration commonly appears first upon the face and breast, and later the entire surface of the body becomes bedewed with moisture, which in many cases flows in streams and saturates the bedclothes. During this stage the urinary secretion again becomes abundant; it is of high specific gravity, and deposits a brick-dust sediment of urates upon cooling.

The three stages of a paroxysm of intermittent fever do not bear any necessary relation to each other. That is to say, the hot stage cannot be considered as a simple reaction after the rigor, and the sweating stage as a necessary sequence of the febrile movement. This is shown by the fact that the cold stage may be entirely suppressed, or that a very severe and protracted rigor may be followed by a brief hot stage; again, the sweating stage may be wanting, the fever gradually subsiding without perspiration, and it is alleged that in exceptional cases the whole paroxysm has consisted of a sweating stage only.

The form of malarial fever known in malarial regions in this country as "dumb ague" receives this name to distinguish it from the common form known as "shaking ague," from the fact that the rigor is absent. It is especially common among the permanent residents of malarious regions.

In young children the cold and sweating stages of intermittent are not so well marked. Rigors do not occur, but the commencement of a paroxysm is often marked by coolness of the surface, lividity of the lips and nails, and not infrequently by a disposition to sleep. The respiration is shallow and frequent, the pulse small and extremely rapid. At the commencement of the hot stage convulsions sometimes occur. The quotidian type is by far the most frequent in young children, and the intermissions are often not well marked, the child remaining fretful or disposed to take an unnatural amount of sleep and declining food.

SPECIAL SYMPTOMS.—*The tongue* is more heavily coated in the quotidian type and in sthenic cases than in asthenic constitutions and in the tertian or quartan types; indeed, it frequently happens in these that the tongue is nearly clean during the paroxysm as well as during the intermission (Morehead).

The tongue in this and in other forms of malarial fever presents certain characters which have been claimed by Dr. Osborn, of Greensboro, Ala.—who first called attention to the subject—to be pathognomonic. The following is his account of the appearance referred to:

> The sides or edges of the tongue are flattened, pinkish, and traversed by sharp lines, creating the impression to the eye of the observer that the parts are crenulated, striated, corrugated, puckered, or crimpled—either term having a shade of appropriateness—but which upon close inspection will be found situated in the substance of the tongue, leaving the mucous membrane even and smooth to both sight and touch.[1]

This appearance of the tongue in remittent fever is referred to by Dr. Baruch, of New York City, as follows:

> The tongue presents a characteristic appearance. It is rapidly overcast by a more or less dingy coating, sometimes brown, but more commonly leaden-hued. Its chief characteristic, however, is the rounding of the edges, and their being marked by alternate ridges and depressions, which are sometimes irregular, giving the appearance of puckering, while to the touch the edges are smooth.[2]

Professor Bemiss, of New Orleans, in reply to a letter from the writer asking information upon this subject, says:

> While differing somewhat from Dr. Osborn in the description of the "malarial tongue," I freely accord him the credit of first calling the attention of the profession to it . . . I do, however, teach students to look for a tongue enlarged, marked on its edges by the teeth, and presenting a dull white or slightly bluish-white tinge on the dorsum, as indicating the presence of malarial poison.[3]

The spleen, in common with other viscera, becomes engorged during the rigor of an intermittent paroxysm; and, either because of its peculiar structure, or because it is specially implicated through its nervous supply, or otherwise, the congestion of this organ is more decided and constant than in the case of the other viscera.

As a result of repeated attacks, or even in chronic malarial cachexia without intermittent fever, the spleen may become enormously enlarged. In place of its usual weight of six or seven ounces it has been found to weigh eighteen or twenty pounds, and even more than this.

It is well known that the bulk of the spleen varies considerably in health in different individuals, and in the same individual at different times. Thus it is said that it commonly enlarges after a meal, toward the end of the process of digestion. The normal spleen is hidden behind the left lower ribs, but during a paroxysm of intermittent its lower margin extends downward and may be felt below the ribs. Upon pressure in this locality the patient complains of some tenderness. In protracted cases of malarial fever, the organ often occupies the whole of the left side of the abdomen, forming the "ague cake" so well known in malarious regions.

The capsule of the spleen being more yielding in children and young persons, the enlargement during a paroxysm of intermittent is more noticeable than in persons of mature age. The swelling may commence during the prodromal stage, and attains its maximum during the cold and hot stages, receding again during the sweating stage and the period of apyrexia (Hertz). Enlargement of the spleen, of a more permanent character, results not only from repeated attacks of intermittent but also from chronic malarial poisoning unattended with febrile manifestations. This fact has led some authors to look upon the splenic enlargement not as a result, but as a primary effect of malarial toxæmia; and this organ has been considered the depot or receptacle in which malaria lurks during the intervals between the periodic febrile attacks. The splenic tumor, when of considerable size, often falls to the lower part of the cavity of the abdomen, and in consequence of the elongation of the suspensory ligament, the organ is freely movable by external manipulation.

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[1] N. Orl. M. & S. J., July, 1870, p. 638.

[2] The Medical Record, New York, Jan. 5, 1884, p. 3.

[3] Letter dated Feb. 15, 1884.

The view that the spleen is in any way related to the development of intermittent fever is opposed by the fact that after its removal from the body the febrile paroxysms may continue to occur; and by the statements of several authors to the effect that malarial fever, even of a fatal character, may occur without any enlargement of the spleen (?) (Jacquot, Saurier).

A singular case is also narrated, in which a man received an extensive wound of the wall of the abdomen on the left side, through which the spleen escaped; as it could not be returned it had to be removed. The patient recovered from the operation, and had malarial fever afterward, just the same as before, although eventually a postmortem examination showed nothing but the shrivelled rudiment of the spleen left.[1]

Morehead speaks of enlargement of the spleen as a *complication* of intermittent fever—"the most common complication"—and says that it does not usually occur in first attacks, unless they have been badly managed, and several paroxysms have taken place.

The urine, as already stated, is increased in amount during the cold stage. According to Parkes, it is most abundant at the termination of the cold, decreases slowly during the hot and rapidly during the sweating stage. The amount excreted does not seem to bear a direct relation to the amount of fluid ingested. The reaction is strongly acid from the increased amount of uric acid present, and for this reason the urine may be quite irritating. Phosphoric acid is also present in slightly increased amount. Ringer confirms Traube as to the increased amount of urea during the paroxysm, and in a careful study of a case of quotidian ague found that the increase commenced in advance of the rigor and before the thermometer showed any rise in temperature. The maximum increase was at the end of the cold stage or just at the commencement of the hot, and from this point the amount fell during the hot and sweating stages. The amount of urea, in five successive paroxysms, was found to bear a definite relation to the temperature. The total increase varied from two hundred to five hundred per cent. A variation of a single degree in the temperature was attended with a larger excretion of urea at high than at low temperatures. The amount of urea excreted was quite independent of the quantity of urinary water. The excretion of chloride of sodium was also largely increased (five-fold), and this too bore a certain relation to the temperature, although not definite as in the case of the urea.

A remarkable fact observed by Ringer was that when the daily return of the paroxysm was prevented by the administration of quinine, an increased excretion of urea and of sodium chloride still occurred at the hour when the paroxysm was due. A dose of twenty grains of quinine administered at bedtime completely cured the patient so far as the subjective symptoms were concerned. On the following day he had no chill, no rise of temperature, and no perspiration, yet the excretion of urea, of chloride of sodium, and of water was increased as usual at the time of the daily paroxysm. The same thing occurred the following day, but the increase was less in amount. The same fact has been observed by Redenbocker.[1]

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[1] Hertz, in Ziemssen's Cyclopædia, vol. i., p. 645.

The following table, which we copy from Fayrer's work,[2] gives the average specific gravity and composition of the urine during the several stages as determined by M. L'Héritier. The figures given are the average obtained from twelve cases :

	Stage.		
	Hot.	Cold.	Sweating.
Specific gravity	1017.330	1020.304	1022.820
Water	967.520	964.680	961.845
Solids	32.480	35.320	38.155
Urea	9.845	9.015	7.624
Uric acid	0.660	0.980	1.029
Salts and organic matter	21.975	25.325	29.502

The following analysis, made in a case of tertian ague, corresponds with that of Ringer as regards the excessive excretion of urea and of sodium chloride during the cold stage of the paroxysm, but also brings to light an additional fact, viz., that the total amount of urine and of the several solid constituents is less for the twenty-four hours during which the paroxysm occurs than on the non-febrile day :

A Case of Tertian Ague, with Analysis of Urine of the Febrile and Non-febrile Days.[3]—G. J——, aged thirty-three, was admitted into the Seamen's Hospital, under Dr. Ralfe, May 2, 1875, suffering from tertian ague. He had had three fits previous to admission, the first being of a quotidian type, beginning at 11 A.M. ; the third tertian, commencing at 7.30 in the day.

May 3d.—The attack began at 6.45 A.M.; the cold stage lasted three-quarters of an hour, the hot stage one hour and thirty minutes, sweating five hours. The highest temperature reached was during the hot stage—105° Fahr. Ordered mist. expectans, and directions were given to have the urine collected the next day from 4 A.M. to 4 A.M.

May 4th–5th (*non-febrile day*).—The analysis of the twenty-four hours' urine gave the following result: Quantity, 2,800 c.c.; acidity, 2.1 grm.; urea, 50.4 grm.; chlorine, 7.5 grm ; sulphuric acid, 1.6 grm.; phosphoric acid, 2.8 grm.

May 5th–6th (*febrile day*).—The attack commenced at 7.30 A.M., and the sweating stage terminated at 4.23 P.M. The analysis of the twenty-four hours' urine gave: Quantity, 1,990 c.c.; acidity, 1.01 grm.; urea, 37.54 grm.; chlorine, 4.68 grm.; sulphuric acid, 1.3 grm.; phosphoric acid, 2.3 grm.

The following table shows the hourly rate of excretion of the urinary substances during the febrile day :

	Max. temp., Fahr.	Amount.	Urea.	Chlorine.	Sulphuric acid.	Phosphoric acid.
	degs.	c.c.	grm.	grm.	grm.	grm.
Before fit, 4–7.30 A.M	normal.	65	1.06	0.116	0.078	0.13
Cold stage, 7.30–8.10 A.M	104.4	195	4.36	0.936	0.156	0.10
Hot stage, 8.10–10 A.M	105	78	1.86	0.374	0.046	0.09
Sweating, 10–12 noon	103.8	60	1.68	0.144	0.102	0.08
(a) Sweating, 12–4.23 P.M.	103.6	89	2.16	0.267	0.071	0.09
Remission, 4.23 P.M.–4 A.M	98.6	85	1.19	0.127	0.034	0.11

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[1] London Lancet, Aug. 6, 1859.

[2] Op. cit., p. 71.

[3] Med. Times & Gaz., Lond., Jan. 22, 1876.

The urine was collected by Dr. Duncan, the House Physician, who visited the patient every quarter of an hour during the progress of the fit, to watch the temperature and make the patient pass water at the proper time. The standard solutions were prepared by Messrs. Griffin, of Covent Garden.

May 7th (*non-febrile day*).—Ordered five-grain doses of quinine to be taken three times a day. Urine to be collected as usual.

May 8th (*febrile day*).—No attack this day, owing, no doubt, to the effect of quinine; nor did any fresh attacks occur during his stay in hospital, while taking quinine. Analysis of the urine gave the following results: Quantity, 2,380 c.c.; acidity, 2.3 grm.; urea, 49.9 grm.; chlorine, 7.8 grm.; sulphuric acid, 1.7 grm. (?); phosphoric acid, 2.6 grm.

It is interesting to observe that the quantities passed on the non-febrile day, and on the febrile day in which the attack was checked by quinine, closely approximate; and the quantities passed on both days are in excess of those passed on the febrile day which had the regular attack. In the cold stage all the urinary constituents, except phosphoric acid, were increased. The phosphoric acid throughout remained very constant, and varied only fractionally in the different stages of the attack.

Temporary glycosuria during attacks of intermittent fever has been noted by several observers. In 1859 Burdel reported that he had found sugar in the urine of eighty out of eighty-six cases of intermittent fever. It was especially observed in the urine of pregnant and suckling women. As glycosuria has been observed by numerous authors to occur during pregnancy independently of intermittent fever, it may be questioned whether it depended upon malarial poisoning in all of these cases. Many other poisons, and especially those which act upon the nervous system, have been shown to produce a temporary glycosuria, which also occurs in other febrile diseases—*e. g.*, scarlet fever.[1]

Professor Verneuil concludes that malaria frequently engenders glycosuria in one of two forms—one contemporaneous with the attack of fever and transient; the other more or less tardy in its onset, independent of the paroxysm, and in all cases permanent.[2]

Dr. Calmetti[3] has recently recorded the transitory presence of sugar in the urine of five patients out of forty-one cases of remittent and intermittent fever observed in a malarious locality in the vicinity of Tunis. Fayrer also states that his experience confirms the occasional occurrence of glycosuria "with or after malarial fever."

That albumen should occasionally be found in the urine of patients suffering from intermittent fever is to be expected, as they have no exemption from the organic lesions with which this symptom is commonly associated. Indeed, patients with chronic Bright's disease, as with any other chronic trouble which undermines the general health, are especially subject to malarial affections. But aside from this there is evidence that temporary albuminuria may occur during the intermittent paroxysm in cachectic individuals, and it is extremely probable that the congestion of the kidneys, which occurs during the cold stage of ague, and the extra tax placed upon these organs during the entire paroxysm, may, when frequently repeated, give rise to the organic changes in their structure which constitute the disease referred to.

Dr. Schoskouski, who examined the urine for albumen in one hundred and fifty-four cases of intermittent fever—soldiers, treated in the military hospital at Kussan, which is surrounded by marshes—reports that he found occasional albuminuria in more than half the cases. In cases in which there had been frequent relapses and cachexia was developed, albumen was nearly always found. In recent cases, on the contrary, it was seldom met with. According to this author, albumen is more frequently met with in the remittent type, and is more common in quotidian than in tertian fevers.[1]

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[1] See a valuable article by Prof. Oscar De Wolf, in Journal of the Am. Med. Ass., Nov. 24, 1883 (vol. i., No. 20).

[2] Fayrer, op. cit., p. 80.

[3] London Med. Record, July 15, 1883.

THE TEMPERATURE.—As already stated, the rise in temperature in a paroxysm of intermittent begins with or precedes the chilly sensations which inaugurate the cold stage. This rise is said to be slow at first, and to become accelerated about the middle of the cold stage. Slight vacillations occur at the commencement of the sweating stage, but when this is fairly inaugurated the temperature falls steadily until it reaches the normal.

Quotidian Intermittent.

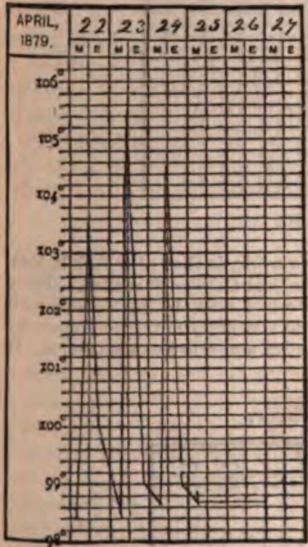

Chart No. 1 (Fayrer).

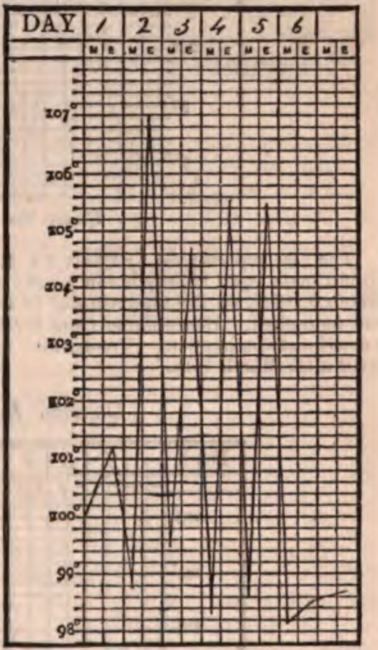

Chart No. 2 (Wunderlich).

The following typical case of quotidian intermittent, with temperature chart, in which the course of the disease was promptly arrested by the administration of quinine, is copied from Fayrer's recent work:[2]

D. P——, East Indian, male, aged thirty-seven years, admitted to Madras General Hospital April 22, 1879. Has had ague since April 19th. Rigors begin at about 10 A.M. daily; fever leaves him about 4 P.M., after profuse sweating. At noon temperature was 103.8°. April 24th, ordered quinine, grs. xv.; 25th, repeated; 26th, quinine, grs. x., bis die; 27th, repeated; 28th, quinine, grs. v., ter die. May 5th, discharged cured.

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[1] St. Petersburg Med. Woch.

[2] Op. cit., p. 88.

Tertian Intermittent Fever.

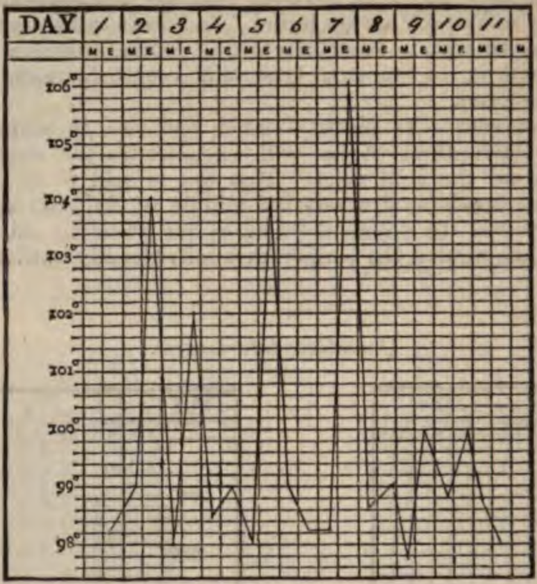

Chart No. 3 (Wunderlich).

The case represented by Chart No. 4, from Fayrer's work, is that of "Rabda Nath, Hindu male, aged twenty-seven years; admitted to Medical College Hospital, Calcutta, March 9, 1881, on the fifteenth day of the disease. He is a cook by trade, well made and nourished. Has suffered from fever for a fortnight; slightly enlarged spleen, and gonorrhœal rheumatism. Treatment: saline diaphoretics and cinchona alkaloids. No fever after March 16th."

Quartan Intermittent Fever.

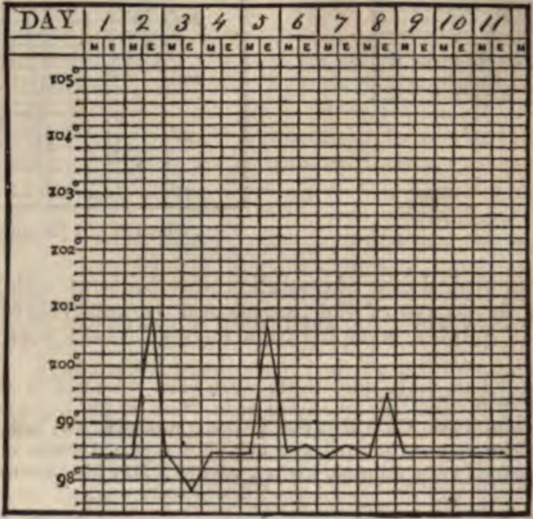

Chart No. 4 (Fayrer).

RELAPSES.—Dr. Wood states that the milder cases of intermittent frequently terminate spontaneously with the seventh or eighth paroxysm, and sometimes as early as the fifth or sixth paroxysm, without any treatment.

More than one-half the tertian intermittents which occurred in the infirmaries of the *Salpêtrière* of Paris in the autumn of the sixth year of the Republic, terminated with the ninth paroxysm, or previously. The treatment was of the simplest kind, and calculated to have little effect upon the course of the disease.[1]

According to Fordyce, quotidians usually end spontaneously in about ten weeks, tertians in about four months, and quartans in six, seven, or eight months. But occasionally these diseases continue for a much longer time, if not interrupted.[2]

But little value can be attached to the periods named by Fordyce, which are doubtless intended to indicate the time during which relapses are likely to occur, rather than that an uninterrupted series of paroxysms occurs during this period.

We have already seen that the primary type, especially in intensely malarious regions, is usually quotidian, and that relapses are apt to be of the tertian or quartan type. Wood says: "Quartans are said to be most apt to relapse." The statement just made is probably more correct, *i.e.*, that relapses are frequently of the quartan type when the primary attack has been quotidian or tertian.

The singular tendency of relapses to observe a septenary period has been noted by numerous observers. Wood says: "In most instances, according to my own observation, the relapse takes place upon the fourteenth day from the occurrence of the last paroxysm; and if this day be passed, then at the end of the third week or at some future weekly period."[3]

The period during which relapses may occur is extremely indefinite, and may be prolonged to several years. It is a very common thing for those who have suffered an attack of intermittent in the autumn to have a relapse the following spring.

Relapses are commonly induced by a secondary cause, but sometimes occur independently of any apparent immediate exciting cause. Doubtless chilling of the surface of the body is the most frequent cause, and those who are subject to attacks of intermittent soon learn by experience to avoid the damp night-air, exposure to cold winds, etc. Next to this we may place exposure to the direct action of the sun's rays—in tropical countries—indigestion, and fatigue.

COMPLICATIONS.—Intermittent fever may be complicated with more or less acute inflammation of the gastric or intestinal mucous membrane, with bronchitis, pneumonia, inflammation of the liver, and, in short, with acute or chronic inflammation of any of the viscera. No doubt the visceral congestion which occurs during the cold stage of an intermittent has a tendency to aggravate an existing inflammation; and it may be that inflammation may be an immediate result of the intense local hyperæmias which are such common, and indeed constant, results of malarial poisoning. But there is no satisfactory evidence that malaria, by its direct action, gives rise to these local inflammations, and we must therefore reject the terms "gastric intermittent," "cerebral intermittent," etc., which have been employed by certain authors.

The cough, dyspnœa, and bronchial catarrh which are said to occur in certain cases during the cold stage of an intermittent, to diminish gradually during the sweating stage, and to disappear entirely during the intermission (Hertz), are evidently due to hyperæmia of the bronchial mucous membrane of a temporary nature, and can scarcely be called bronchitis, although it is easy to believe that it might develop into bronchitis. The same may be said of the intestinal flux which in certain cases seems to take the place of the usual transpiration from the cutaneous surface.

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[1] Dict. de Méd., xvi., p. 589.

[2] Wood's Practice of Medicine, vol. i., p. 259.

[3] Op. cit., p. 259.

An eruption of *herpes*, which appears usually upon the lips and other parts of the face, is of frequent occurrence as a complication or sequela of intermittent fever. This eruption may appear during the prodromal stage, during the paroxysm, or even after the disease has been arrested by treatment. According to Hertz, this herpetic eruption rarely occurs more than once during the progress of a case. The same author states that it is more common in the spring than in the autumn, and that occasionally it complicates nearly every case which occurs during an epidemic of intermittent fever.

Morehead states that *hepatic inflammation*, or enlargement, as a complication of intermittent fever, has been of rare occurrence in his experience in India. Temporary congestion of the liver and consequent derangement of its function is, however, one of the most common symptoms of malarial disease, especially of the quotidian or remittent type.

Jaundice is an occasional complication of intermittent, but is far more common in remittent fever.

Affections of the stomach and bowels are the most common complications of intermittent, especially in chronic cases in asthenic subjects. According to Morehead, sthenic Europeans rarely suffer from diarrhœa or dysentery during an attack of intermittent, unless they are in the habit of spirit drinking, or irritability of the stomach and bowels has been induced by the injudicious use of purgatives.

Dysentery as a complication of intermittent fever is very common in regions where both diseases are prevalent; but as Colin has pointed out, certain intensely malarious regions are comparatively exempt from this complication, which seems to depend upon special conditions quite independent of those which produce malaria, although often associated with them. Thus the author mentioned says that in certain parts of Algeria dysentery is a complication which carries off large numbers of the victims of malarial poisoning, whereas in Rome it is not more common than in Paris, and influences the mortality from malarial diseases but slightly.

Morehead remarks: "When *diarrhœa* coexists with intermittent fever, a tendency in the febrile accessions to alternate with diarrhœa may occasionally be noticed; the one being present for three or four days, then ceasing, and being succeeded by the other; . . . but it is generally a character of old fever cases, not of recent ones."[1]

A *scorbutic taint*, as indicated by sponginess and discoloration of the gums and a tendency to hemorrhages, is mentioned by Morehead and Fayrer as a frequent complication of intermittent fever among the natives of India. The common occurrence of this complication among troops during an active campaign, and especially in our own armies during the late war, has been insisted upon by Woodward.[2] No doubt scorbutic subjects are especially subject to intermittent fever, and the combined influence of malaria and of the conditions which give rise to scurvy very quickly develops a condition of cachexia, in which the power of resisting further exposure to the malarial poison or other morbific influences is greatly reduced.

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[1] Op. cit., p. 48.

[2] Camp Diseases, Philadelphia, 1863.

The combination of the symptoms of malarial poisoning with those of typhoid fever, yellow fever, or other specific febrile affections is commonly regarded as a malarial complication occurring in the course of these diseases, or accompanying them throughout, from previous exposure to malarial influences, and not as a typhoid complication, etc., of the malarial disease. A consideration of "typho-malarial" fever, therefore, does not come within the scope of the present treatise, any more than do the idiopathic inflammations and various accidents which may occur during the course of an intermittent fever.

SEQUELÆ.—The most frequent result of repeated attacks of intermittent, or of the continued action of malaria not attended with febrile manifestations, is that condition known as *malarial cachexia*. This is characterized by anæmia, feeble circulation, impaired digestion, debility, and an enlarged spleen. In addition to this there is often enlargement and functional inactivity of the liver, dropsical effusions, hæmic murmurs, hurried respiration, mental torpor, and in some cases albuminuria.

The anæmia is often profound; the patient has a blanched appearance, the conjunctivæ have a pearly lustre, the lips are pallid, and the slightest exertion causes dyspnœa and palpitation of the heart. Sometimes the skin has a bronzed or icteric hue.

A systolic cardiac murmur is not unfrequently observed in these cases of malarial anæmia, and Morehead has pointed out that this may be associated with abnormal præcordial dulness, although there is no organic heart trouble. This dulness is said to be "produced partly by displacement of the heart upward, and partly by the enlarged spleen preventing the free descent of the diaphragm and the full expansion of the lung, with complete overlapping of the left side and base of the heart by its thin edge."[1]

Respiration may be embarrassed by œdema of the lungs, or asthma of nervous origin may be developed, and this is liable to produce emphysema and chronic bronchial changes (Fayrer).

The victims of malarial cachexia suffer greatly from dyspeptic symptoms; the tongue is commonly more or less coated, the appetite poor and capricious, digestion feeble and the bowels deranged, diarrhœa being more common than the opposite condition. The enlarged spleen and liver, and the meteorism which is so common in these cases, produce a tumid, protruding abdomen, which is the more striking and apparent when the patient is stripped, from the attenuated limbs and well-defined ribs, due to muscular atrophy.

Chronic Bright's disease may doubtless result from repeated attacks of intermittent fever, as may also organic changes in the structure of the liver. As a result of these organic lesions we may have local or general dropsical effusions.

Fayrer says that there is a strong tendency to the formation of fibrinous coagula in the heart and arteries in these cases of malarial cachexia. He has often seen a limb in peril from the plugging of its main artery.

The susceptibility of these patients to urethral fever from catheterism is also mentioned by the same author, who says: "The mere passage of an instrument will in some cases produce a severe attack of rigors followed by fever and sweating, and it may give rise to symptoms of a pyæmic nature."[2]

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[1] Op. cit., p. 36.

[2] Op. cit., p. 79.

Sequelæ connected with the nervous system may accompany those already mentioned, or may remain as evidence of a former intermittent when the general health has been restored. Of these, neuralgia in one or the other of its protean forms is by far the most common. Paralysis, epilepsy, and insanity may no doubt also result, in exceptional cases, from severe or repeated attacks of intermittent fever.

Retinal hemorrhages and deposit of pigment in the course of the retinal vessels may give rise to defective vision. Amaurosis is also an occasional sequela of intermittent.

Apoplexy of the spleen, with rupture and escape of blood into the cavity of the peritoneum, occasionally occurs as a result of the extreme distention of this organ during the cold or hot stage of an intermittent paroxysm (Hertz).

MASKED INTERMITTENTS (*Fièvres Larvées*).

Intermittent attacks due to malaria, and curable by quinine, not presenting in a definite manner the characters which are recognized as belonging to simple intermittent as heretofore described, have been designated "masked intermittent."

The febrile movement in these imperfect or abnormal intermittent attacks is often slight or altogether absent, and the phenomena are for the most part of a nervous character, and commonly consist in periodic attacks of neuralgia, which in certain cases precede, alternate with, or follow regular paroxysms of intermittent.

These neuralgic attacks commonly assume the quotidian type and occur for the most part in the morning. They are located by preference in the branches of the trigeminus, and especially in the frontal branch of the ophthalmic division (Hertz). There is often a slight chilly feeling at the outset of an attack, and the thermometer may indicate a trifling increase in temperature. Supra- or infra-orbital neuralgia is associated with throbbing pain on the same side of the head, with injection of the conjunctiva, lachrymation, and swelling of the upper lid. The duration of an attack is from half an hour to three or four hours and the pain is often intense.

Other nerves may be implicated—the superior or inferior maxillary, the intercostals, the sciatic—and a variety of intermittent nervous phenomena have been described other than the painful affection known as neuralgia.

Colin speaks especially of an intermittent urticaria, and Hertz has given a long list of symptoms of masked intermittent, including anæsthesia along the course of various nerves, intermittent paralysis, clonic and tonic spasms, hysteriform and chorea-like seizures, maniacal attacks, intermittent hyperæmia, hemorrhage, coryza, bronchial catarrh, etc.

There can be little doubt that the symptoms referred to have in many cases been improperly ascribed to malarial poisoning. Trousseau especially has insisted that intermittent nervous phenomena are not uncommon quite independently of this cause. He says:

> There can be no doubt that the periodic type is observed in a multitude of chronic affections very distinct from the paludal class, and that cinchona modifies or suspends this symptom without affecting the nature of the morbid state thus manifested. . . . Let us also call to mind certain facial neuralgias which are wholly independent of paludal disease, and which, when their attacks are regular, have perhaps no more potent curative, or at least palliative modifier, than sulphate of quinia. . . . Migraine is also often periodic. . . . We have treated, in the course of a year, two intermit-

tent urticarial fevers, one quotidian, one tertian, both with accesses toward evening. The patients never had been exposed to the action of paludal miasms. Bleeding and evacuations were without appreciable effect. Sulphate of quinia had an immediate and complete effect.[1]

Colin also protests against ascribing all of these intermittent nervous phenomena to the action of malaria. He says:

> We are astonished to see Griesinger admit as masked fevers (fièvres larvées) the most diverse nervous affections: convulsions localized or general (choreic or epileptiform) hysteria, amblyopia, temporary paralysis of some of the members, and even symptoms of a very different order, such as partial or general œdema.[2]

PERNICIOUS INTERMITTENT.

When from the poisonous action of malaria upon the blood and nervous centres, or from the local congestions which result from such action, symptoms threatening life are developed, an intermittent fever is said to be "pernicious."

The pernicious nature of an attack may depend upon exposure to the exciting cause in an intense or concentrated form—*e.g.*, in tropical swamps; upon secondary causes acting in conjunction with the malarial poison—*e.g.*, insolation, alcoholism; or upon feeble resisting power due to previous illness or individual peculiarities.

The difference between simple intermittent and pernicious intermittent is a difference in degree only, and of two persons who are exposed in precisely the same way, one may have a simple ague and the other a pernicious attack characterized by unusual algidity and depression of the heart's action, by coma, or by exhausting discharges, etc.

But individual susceptibility to the action of malaria is very rarely so great as to give rise to pernicious symptoms in temperate regions—the New England and Middle States, for example—and it is only in the southern parts of our own country and in tropical and sub-tropical regions generally that these fevers prevail. Where the conditions are extremely favorable for the generation of malaria, as in certain tropical swamps, no constitution is strong enough to resist the deadly effects of the poison, and exposure for a single night almost inevitably gives rise to pernicious symptoms and to death unless the patient is rescued by the timely administration of the antidote.

Simple intermittent fever may endanger the life of feeble or aged persons by the persistent return of the daily paroxysm or by its duration and intensity, but so long as the symptoms are only such as belong properly to an intermittent paroxysm, as heretofore described, the fever is not considered pernicious. Final failure of the heart's action or of the functional activity of other organs from protracted intermittent is an occasional result of chronic malarial poisoning. Pernicious symptoms, on the other hand, are developed in acute malarial toxæmia, and are evidence that the nervous centres have been overwhelmed by the intense action of the poison.

The pernicious character is not, however, always seen at the outset. Indeed, it is more frequently the case that two or three paroxysms of simple intermittent occur before the alarming symptoms of "pernicious fever" are developed.

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[1] Op. cit., p. 161.

[2] Op. cit., p. 194.

Whether these symptoms are to be ascribed to an increased production in the body of the poison which gives rise to the intermittent paroxysms, or to a diminished resistance on the part of the nervous centres to the effects of this poison, it is impossible to determine, in the absence of any definite knowledge as to the real nature of this poison.

Intermittent fevers which are dangerous to life because of accidental complications are not properly called "pernicious intermittents," this term referring solely to the dangerous symptoms induced by the malarial poison. A fever, therefore, which is dangerous by reason of complication with typhoid fever, with dysentery, with a scorbutic taint, or with septic poisoning, is not a pernicious *malarial* fever, although these fevers, resulting from the combined action of another morbific agent with malaria, are frequently spoken of also as "pernicious fevers." Still less does a local inflammation occurring during the course of an intermittent fever justify the use of this term. Hepatitis, gastro-enteritis, meningitis, etc., may occur as complications of intermittent fever, but the pernicious character is quite independent of any such complication, although it is manifested by symptoms relating to the functional activity of the brain, the heart, and the various organs concerned in vital processes. These symptoms all point to a paralyzing effect of the poison upon the nervous centres, and they differ according as this paralyzing effect is manifested most intensely by the cerebro-spinal or by the ganglionic nervous system. The two leading forms of pernicious fever under which the different varieties described by various authors may for the most part be grouped are the *algid* form and the *comatose* form. With the first-named we would group the *syncopal*, the *cardialgic*, the *choleraic*, and the *diaphoretic* or *sudoral;* with the last the *delirious*, the *convulsive*, the *apoplectic*.

This classification does not include the *hemorrhagic* or the *icteric* types of pernicious fever which have been described by some authors. Occasional hemorrhages occur in all the types of malarial fever, but we know of no hemorrhagic type of malarial fever, properly so called, in which the pernicious character of the disease in its primary stages is due to a tendency to loss of blood. The "hemorrhagic malarial fever" which we shall describe hereafter is one of the later manifestations of malarial poisoning in cachectic individuals. The hemorrhagic malarial fever of some writers is unquestionably nothing more nor less than yellow fever, which has repeatedly been described as a malarial fever under various local names.

Pernicious fever may occur repeatedly in the same individual. Sullivan, who has had much experience in malarial regions, says: "I have known persons whose life was always a burden to them from fear of a fresh attack."[1] The same author mentions as predisposing causes "all chronic diseases of tropical climates, all deep-seated causes of debility, privation, and suffering, the emotions from grief or anxiety, and alcoholism." To this should be added the effects of heat, either from exposure of the head to the direct action of the sun's rays or from an elevated external temperature continued day and night, as is so commonly the case in the tropics, and especially when evaporation from the surface is retarded by saturation of the atmosphere with moisture.

The fact that pernicious attacks occur almost exclusively during the season of greatest heat and of the most abundant evolution of malaria is well shown by the observations made in Rome by M. Colin during the French occupation of that city. This author says:

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[1] Dr. J. Sullivan: Pernicious Fever, Med. Times & Gaz., March 11, 1876.

> In general the occurrence of a pernicious attack, at least among individuals placed in the conditions of our army in Rome, takes place only during the endemo-epidemic period, from the commencement of July to the end of the month of November. A pernicious fever during the first six months of the year has always been a rare thing in our military hospital, and has not even been observed in my service. The following figures show that the same is true among the civil population. Thus out of 281 cases of pernicious fever treated in the hospital of the *Saint-Esprit*, we find that 8 occurred in January, 1 in February, 2 in March, 4 in April, 2 in May, 2 in June, 38 in July, 102 in August, 67 in September, 30 in October, 15 in November, and 10 in December. That is to say, there were 262 cases during the second six months and only 19 during the first. The still more complete absence of pernicious fevers in our army during the first six months was due to the fact that we sent a large number of convalescents to France.[1]

The same author has studied the relative frequency of these pernicious attacks as compared with those of simple intermittent. This was in 1864 as one to twenty among the civil population, as shown by the records of the hospital *du Saint-Esprit*, and as one to twenty-five among the French soldiers admitted to the hospital *Saint-André*. The official medical statistics relating to the French troops in Algeria give about the same proportion. This proportion is often greatly exceeded in highly malarious localities in the tropics, while, as already stated, it becomes reduced to zero in northern temperate regions.

What has already been said shows clearly enough that relapses occurring after the season of prevalence of primary attacks, or after removal from a malarious region, are not likely to present pernicious symptoms.

The *prodromes* of pernicious fever do not usually differ from those of simple intermittent; but in exceptional cases it is said that the dangerous character of the approching paroxysm is indicated by drowsiness, dizziness, convulsive twitching of the muscles, severe headache, epigastric pain, or incessant vomiting.

Simple intermittent may gradually assume the character of pernicious fever, the successive paroxysms increasing in severity and in the threatening nature of the local congestions, or a pernicious attack may immediately follow a simple one which had presented no unusual or alarming symptoms.

In tropical regions it not unfrequently happens that the first attack in a previously healthy individual after an unusually dangerous exposure is of a pernicious and even fatal character. But in our own country this is a rare event, and the rule is as previously stated, viz., that one or more simple paroxysms first occur. This is true also in the vicinity of Rome, although Colin states that it occasionally occurs that persons are seized at once with a pernicious attack after crossing the Pontine Marshes at night.

According to Hertz, the pernicious attack in the quotidian type is usually after the second to the fifth day, and in the tertian type still later, sometimes not until the end of two or three weeks. It seems probable that pernicious symptoms which are delayed so long as this are due to continued or renewed exposure in a malarious locality or to a secondary cause.

All authors agree that pernicious symptoms are almost unknown in the quartan type of intermittent fever, which we have seen belongs almost exclusively to temperate latitudes. And in accordance with the law that types of a shorter period are more common as we approach the tropics, we find that the tertian type gives a comparatively small proportion of pernicious attacks, the quotidian a larger proportion, and remittent fever the largest of all. There is reason to believe that "pernicious continued fevers" have for the most part a different etiology, and that they have been improperly ascribed to the malarial poison. Dr. Davidson, of New Orleans, says that pernicious fever, though often quotidian, is more frequently of the tertian type. This is no doubt true in those latitudes where this is the prevailing type, and agrees with the observations of physicians in central Europe. The same author says that, according to his observations, "the third paroxysm is the one in which most commonly the pernicious phenomena present themselves, though instances occur of the algid form in which no reaction takes place from the first chill, the patient dying in that paroxysm."[1]

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[1] Op. cit., p. 208.

Sullivan says:

> There are two symptoms which, when they occur in the course of an intermittent, always occasion me great alarm and anxiety. The one is an acute pain which fixes itself in some part of the body—sometimes in the side, like an attack of pleurisy; at others it strikes upon the hip-joint. Now from long experience I have always found the accession of these pains to be a very ominous symptom. The second symptom is the vomiting of blue (not black) matter; it may occur in the adult who has suffered from marsh cachexia or from chronic diarrhœa. . . . In children when fever is ushered in by general or partial convulsions, the symptom is generally fatal, as indicating a tendency to the same manifestation in every succeeding attack.[2]

The author last named has had an extended experience in the West Indies, and has contributed some valuable papers to the literature of malarial diseases. But we suspect that the value of his observations relating to "pernicious fever" in the city of Havana (*loc. cit.*) is somewhat vitiated by an error very commonly made in that city, where yellow fever is endemic and where the pernicious symptoms due to the yellow fever poison, either complicating or independent of malarial infection, are often improperly ascribed to malaria, or simply named "pernicious fever," without any exact idea as to the etiology of the disease so named.

The popular fallacy, shared to a large extent by the physicians of Havana, that Creoles and their children are exempt from the effects of the yellow fever poison, is so generally believed that a fever attended with back vomit, suppression of urine, and a yellow skin, when it occurs in an individual of this class, almost invariably receives some other name than yellow fever. Our suspicion that Sullivan has also confounded pernicious symptoms due to yellow fever with those produced by the malarial poison is based upon the following statement in his paper already referred to:

> In the tropics pernicious fever may be seen in all its most formidable array, *complicating* the various types of intermittent and tending to aggravate a variety of morbid states *which have no necessary connection with the poison of malaria*. The prognosis must depend upon several conditions. *Suppression of urine* is an alarming symptom, but should the secretion be restored an improvement is sure to follow. Convulsions, frequent in children, are perhaps, *next to black vomit*, the most dangerous symptom; when they make their appearance at the close of an attack of fever there is always danger to life. *Vomiting of black matter* is fatal to adults; I have seen children occasionally recover.

The pernicious attack is sometimes developed with astonishing rapidity, the patient passing from a condition of apparent safety to one of imminent danger within a very short time. Thus Colin says that during his visits to the wards of the military hospitals in Rome he has several times found patients in an unconscious condition, who a few moments previously had been in conversation with the attendants, without giving any indication of the imminence of the pernicious attack. In other cases an incoherence of ideas will be noticed, and there may be a certain mental exaltation, shown by volubility, or the patient may be taciturn and the mind sluggish. The author last mentioned says:

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[1] N. Orl. M. & S. J., Feb., 1880, p 750.

[2] Med. Times & Gaz., Lond., March 11, 1876.

> The first patient I lost from a pernicious paroxysm left upon my mind, the morning of the day upon which he succumbed, a strange impression, from the air of calm satisfaction imprinted upon his face, and from the slowness of his replies to my questions, notwithstanding the fact that he was entirely free from fever. I have seen pernicious attacks carry off patients of whom the attendants had complained, some hours before, because of their indocility and the coarseness of their replies to questions, sometimes even because of acts of brutality, which seemed to depend less upon a veritable delirium than on a momentary eccentricity. In other cases sleep during the night has been interrupted by frequent sighs.[1]

ALGID PERNICIOUS INTERMITTENT.

In this form of pernicious fever the alarming symptoms seem to be due entirely to the action of the malarial poison upon the nervous system, and especially upon the vaso-motor nerves. In the comatose form, on the contrary, the pernicious symptoms are often due to secondary causes—insolation, alcoholism. It is for this reason that algid pernicious fever prevails during the whole season of malarial evolution, in the autumn as well as in the summer, while the comatose form is more common during the season of greatest heat.

The pernicious attack frequently presents at the outset the characters of an ordinary intermittent paroxysm; the chill occurs as usual, but instead of the usual febrile reaction the patient continues to grow cold, although complaining of intense thirst and burning heat within. The skin becomes livid and cold to the touch, the limbs and forehead feeling like marble; the temperature in the mouth may fall several degrees below the normal (as low as 86° to 88° Fahr.—Hertz); the lips are colorless. The tongue is commonly pale, broad and flat, the edges indented by the teeth, and coated with a thick and whitish fur (Davidson). The tongue is the last to become cold, and when the air expired is colder than that inspired (?), the danger becomes imminent (Sullivan). The pulse is small and thready, often irregular, and may be frequent or greatly retarded—as slow as forty in a minute (Hertz). In some cases it cannot be felt at the wrist, although the heart is beating strongly and tumultuously, "as if laboring hard to upheave and dislodge the mass of blood by which it is oppressed" (Sullivan). Respiration is shallow and rapid or very much reduced in frequency—as slow as ten in a minute (Hertz). "If no effort at reaction succeeds and remedies fail to bring it about, the respiration becomes slower and sighing, the cerebral functions give way, the countenance becomes hippocratic, hiccough takes place, and the patient gradually sinks into death" (Davidson). Vomiting is a common symptom; the fluids taken into the stomach are quickly rejected, and in the absence of any ingested material a little mucous, occasionally tinged with bile, is ejected. The bowels are commonly freely moved, the dejections being copious and watery, and sometimes pinkish in color, "resembling the washings of putrid meat" (Davidson). The urine is of high specific gravity, dark-colored and scanty. The mind remains clear, although somewhat torpid, and the patient is anxious and apparently conscious of the gravity of his condition. The pupils are dilated and the eyes expressionless (Hertz). Colin says that while the intelligence is intact and the patient feels that he is dying, his countenance is without mobility and impassive.

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[1] Op. cit., p. 226.

> Nothing is more striking than the immobile countenance of these patients, whose expression is that of repose, of tranquillity, which would scarcely cause the physician to stop by the bedside were it not that in seeking the pulse, as a matter of habit, he is struck by the glacial cold of the skin and the arrest of the circulation.[1]

The algid condition does not give to the patient the sensation of cold which he experiences in an ordinary rigor when the thermometer shows that the temperature of the body is really above the normal. On the other hand, he complains of internal heat and of intense thirst. Owing to the perverted nervous condition, heat applied to the extremities is disagreeable to the patient; even the warmth of the hand is unpleasant (Davidson). The skin soon becomes bathed with a cold, clammy perspiration.

In non-fatal cases reaction occurs after a time, the pulse gradually regains its strength and volume, the normal temperature of the body is reestablished, gastric irritability is relieved, and the patient may fall asleep. The intermission is characterized by a greater amount of exhaustion and nervous prostration than is usual after an ordinary paroxysm of intermittent, and if a return of the pernicious symptoms is prevented by prompt and active medication, still convalescence is not usually established at once. It is attended sometimes with headache, dizziness, irritability of temper, and occasionally with partial loss of memory; and in some cases a typhoid condition supervenes, like that after cholera (Hertz). Unless promptly arrested by treatment, the pernicious symptoms reappear at the next paroxysm with increased gravity, and a second or third attack of this character is commonly fatal.

The following case is reported by Sullivan in his article on "Pernicious Fever," already referred to:

> The most remarkable case of algid pernicious fever that I ever witnessed was the following: In the present year (April, 1875) I was called to visit the wife of D. B. M——, a well-known sugar planter in Cuba. She had been delivered of a child about two months before, at which time she complained of slight chills and fever; since then severe intermittent had set in. I was greatly surprised, on my arrival, at the consternation and dismay depicted on the countenances of the patient's friends and attendants. I decided upon taking a view of the patient unseen by her. She was seated in an arm-chair, the arms of which she firmly grasped with both hands, the body slightly inclined forward, rigid, erect; the face was pale and cadaverous, the countenance expressive of anxiety and terror, mixed with a certain degree of sadness. She looked as it were on vacancy, and took no notice of those who surrounded her. On my entering the patient's room she directed an anxious and inquiring look toward me, as if conscious who I was and desirous to be relieved. I took her hand, which, as well as the entire body, was bathed in a cold, clammy, icy sweat; no pulse at wrist. She could only reply to my questions in a whisper, but a whisper deep, cold, and unearthly. The heart's beat was strong and even tumultuous, as though laboring hard to upheave and dislodge the mass of blood by which it was oppressed The right heart communicated its impulse to the jugular veins—hence strong venous pulsations.
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> I found, on examination, considerable congestion and enlargement of the spleen, and induration of an atrophied liver. I ordered a hot mustard foot-bath, ten grains of calomel with fifteen grains of quinine, to be taken immediately, the dose to be repeated in two hours' time; frictions of quinine and brandy (two to six drachms) to be rubbed over the extremities and down the spine every half hour. About four hours after my first visit the heat of the body returned, and the patient was enabled to lie down in

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[1] Colin, op. cit., p. 249.

her bed, which she had not been able to do during the last three weeks. After the second dose I followed up the quinine and calomel in smaller proportions—two grains of calomel to four of quinine every four hours. I ordered besides, in order to promote the partially suspended secretion of urine, two tablespoonfuls of a strong diuretic mixture every two hours, and placed over the loins (a custom peculiar to the country people) some digitalis wetted with vinegar. After eight hours had elapsed considerable relief was obtained, and all the symptoms improved; the secretion of urine was restored, circulation became less impeded, and some sleep was procured. The algidity returned daily about 3 P.M. for three successive days, but in a gradually milder form of less duration, and the patient finally recovered.

In the *diaphoretic* or *sudoral* form of pernicious fever algidity is less marked at the outset, and the pernicious character is shown by extreme diaphoresis, attended with symptoms of collapse, during the sweating stage of an intermittent paroxysm, which may otherwise have been normal. The sweating may continue during the intermission, and is attended with increasing feebleness of pulse and coldness of the surface, with intense thirst, and unless reaction is established ends in death.

This form is quite rare, and it should be considered rather as a variety of algid pernicious fever than as a distinct type. Torti, who himself nearly succumbed to an attack of this kind, remarks that it is the most treacherous of all forms of pernicious intermittent, for as the dangerous phenomena are only developed after a febrile paroxysm has gone through its regular course, the physician is apt to think that his patient has passed the critical period and is beyond danger.[1] This form of pernicious fever does not depend upon the external temperature, and attacks, by preference, the victims of malarial cachexia. Colin states that it is more common in the autumn than during the heat of summer. This author gives the following case:

Tertian Intermittent Fever; Sudoral Pernicious Attack.—Gieulles, grenadier in the Seventy-first Infantry; in Italy four years; admitted twice to the hospital of Velletri, during the summer of 1864, for tertian intermittent. Upon being attacked a third time he was sent to Rome and admitted, September 12th, to the hospital of Saint-André (No. 109).

On September 15th, at the moment of our afternoon visit to the wards, the patient was attacked with a paroxysm of fever for the first time since his admission to hospital. He was in the cold stage and complained especially of headache. The following morning we learned that Gieulles, having gotten up during the night, had fainted. We found him inundated with sweat, the skin cool, the voice almost extinct, and in a state of complete muscular inability. *Prescription:* Potion with two grammes of tannin, to be taken by spoonfuls. The patient swallowed at once in our presence one gramme of sulphate of quinine in solution; eight decigrammes were given an hour later.

In the evening there was a notable improvement. The patient's bed was changed because of the abundance of the perspiration, which, however, had diminished in quantity; the skin had resumed its normal temperature. Five decigrammes of sulphate of quinine were administered.

The perspiration continued, but without fever and in less degree, during the two following days. From that time a progressive improvement occurred, and October 18th the patient was sent to France.[2]

The *cardialgic* form of pernicious intermittent is a variety of algid pernicious fever in which during the stage of chill the patient is seized with intense pain in the region of the stomach, attended with nausea and vomiting. The pain is burning, darting, or spasmodic in character, and radiates from the epigastrium in the direction of the attachments of the diaphragm. According to Colin, the pain, the anxiety, and the attitude of the patient call to mind the symptoms of acute pericarditis, or of diaphragmatic pleurisy of a grave character. The author named states that the attacks may occur during any stage of an intermittent paroxysm, or even during the intermission.

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[1] Therap. spec., lib. iv., cap. ii.

[2] Op. cit., p. 262.

The invasion is sometimes so abrupt that the patient, suddenly aroused from sleep by the epigastric pain, sits up in bed, leans forward and seizes upon the bedclothes for the purpose of giving a point of support to the muscles concerned in inspiration. The respiration is sometimes nothing more than a succession of convulsive sobs or long sighs, interrupted by attempts to vomit. The face is pale and anxious, the skin cold, the pulse small and frequent. A physical examination of the chest shows that the lungs are intact.

Colin gives the following case :

Fever first Remittent, then Quotidian Intermittent ; Cardialgic Pernicious Attack ; Recovery.—Choussard, private Nineteenth Infantry ; in Italy three years, stationed in the quarter Sainte-Agathe ; admitted to hospital July 22, 1864 (in our service at the military hospital of Saint-André ; No. 118).

This patient was attacked with simple remittent fever which accomplished its normal evolution. After August 7th a paroxysm of quotidian intermittent occurred regularly between seven and eight o'clock in the morning. A daily dose of eight decigrammes (12 gr.) of sulphate of quinine was administered. The fever was arrested August 14th. Two additional doses were administered, of five decigrammes each, on August 15th and 17th.

At our visit, on August 17th, our attention was attracted by the cries and the attitude of this patient. Leaning forward in bed, his regard fixed and anxious, he seemed to respire with the efforts of a man placed in a vacuum. The inspiration was noisy, plaintive, interrupted by sobs, followed sometimes immediately by hiccough and bilious vomiting. This condition had lasted from two o'clock in the morning, and the patient indicated as the seat of his pain the epigastrium, by digging into the skin in this region with his finger-nails. His face was pale, the skin cold, the pulse small and frequent. He had neither cephalalgia nor a sensation of cold ; for him the cardialgia was the only symptom. *Prescription :* Warm drinks, an ethereal potion, and an enema containing opium and two grammes (30 gr.) of sulphate of quinine. "During the day the vomiting became more frequent and more abundant, two attacks of syncope occurred, and the house physician had prescribed a potion of acetate of ammonia (15 grm.) which had been rejected, and some sinapisms.

On August 25th, at the time of my visit the pain had been somewhat relieved ; the patient could lie down in bed, and we found him reclining on his left side, the body curved forward ; the groaning still continued and the pulse was feeble and frequent. *Prescription :* Ice, to be swallowed ; two grammes of sulphate of quinine in an opiate enema ; a blister to the epigastrium. At the evening visit, the symptoms were all less severe ; intense orthopnœa ; the patient seizes his mattress with both hands to aid his efforts at inspiration ; tendency to syncope. Vomiting has ceased, and the patient was able to swallow in our presence eight decigrammes of sulphate of quinine in solution.

August 26th.—The patient is very feeble, and replies to questions with difficulty, in a low voice ; but there is a considerable improvement in his condition. He can lie upon his back without experiencing epigastric distress. He complains especially of faintness. Algidity still remains in the same degree. *Prescription :* Bouillon, coffee, a hot-air bath.

The tolerance of the stomach was complete, and after August 27th the patient was considered out of all danger. But corresponding with this rapid amelioration, commencing the third day of the cardialgic attack, the patient offered a remarkable example of the rapid development of malarial cachexia.

From the evening of the 27th we noted a general œdema, a yellowish tinge of the complexion, a considerable enlargement of the liver and of the spleen. The following days the belly became enormous, as well as the limbs ; and at the time of the departure of the patient for France (September 20th) all of these symptoms persisted, accompanied by a general trembling, which made us fear at each instant a return of the pernicious attack.[1]

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[1] Op. cit., p. 265.

A variety of algid pernicious fever, denominated *syncopal*, has been recognized by several authors. In the state of collapse which results from an attack such as has heretofore been described—algid sudoral or cardialgic—syncope is very apt to occur and may be the immediate cause of death. Indeed simple intermittent fever, in which the several stages are severe and prolonged, may, in exceptional cases, be followed by death from syncope. Fayrer has given an example of this, and points out the danger of an attempt on the part of a patient to rise or make any exertion while still exhausted by a severe and long-continued paroxysm. He says:

> This has been impressed on me by more than one case. A staff officer in Calcutta had just gone through a paroxysm when I saw him—a long hot stage had passed—he lay pale, exhausted, and bedewed with cold, clammy sweat, but felt much relieved and was reading. He expressed a desire to remove into another room, but observing his depressed condition, feeble voice and pulse, I instructed his attendants on no account to allow him to move; shortly after I left he rose, made a few steps, sank, and died on the floor. This collapse is most prone to follow a prolonged hot stage.[1]

Lind has reported examples of sudden death from syncope, in the cases of laborers engaged in digging the earth in the tropics, which he ascribes to the direct action of the malarial poison. Torti also believes that syncope may be the only manifestation of the pernicious character of an attack, the patient dying suddenly in consequence of a slight exertion, such, for example, as turning over in bed. Colin admits the possibility of such attacks from the direct action of malaria in the torrid zone, but says that in temperate climates he is disposed to think that syncope is more commonly an accident of malarial cachexia, rather than an attack comparable to the pernicious fevers, properly so called.

> It is, in short, among individuals exhausted by malarial intoxication of ancient date, among patients suffering from dropsical effusions in the most important cavities of the organism, among those who have softening of the tissue of the heart, that we see these cases of sudden death classed as *syncopal* pernicious fever. It is especially at the end of the season of fevers, in October and November, when cachexias are at their maximum, that these accidents are most frequent.[2]

The state of collapse into which the victim of an algid pernicious paroxysm quickly falls, resembles very closely the collapse of cholera, but the discharges from the stomach and bowels, which are often quite copious, are commonly bilious in character. A form of pernicious fever, denominated *choleraic*, has, however, been observed, which seems to merit this name from the prominence of the choleraic symptoms, and from the fact that the discharges resemble those of true cholera. But it is questionable whether the *choleraic* pernicious fever of authors is properly ascribed to the action of malaria alone. First, we note that this form is most common in regions where cholera also prevails, and there is reason to believe that the endemic prevalence of malarial fevers and cholera in the same territorial limits has led to confusion in this case, just as in the case of typhoid fever and malaria, and of yellow fever and malaria, in regions where these diseases are associated.

The choleraic form of pernicious fever has also been observed in localities far removed from the endemic prevalence of Asiatic cholera; but, as Colin remarks, it is especially during the season of greatest heat, when sporadic cases of cholera are also seen, that these cases occur, and this author very properly ascribes the choleraic symptoms to the meteorological and local conditions which produce *cholera nostras*, rather than to the malarial poison, *per se*. The fact that the choleraic symptoms are an addition to those induced by the malarial poison is further shown by the non-recurrence of these symptoms during successive paroxysms, contrary to the rule in ordinary algid pernicious fever. The collapse of algid malarial fever differs from that of cholera in the absence of cramps and in the facies of the patient, which in the one case is calm and expressionless, and in the other indicates the suffering caused by the characteristic cramps, which are common to both epidemic and sporadic cholera.

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[1] Op. cit., p. 76.

[2] Op. cit., p. 267.

The English physicians in India admit that the symptoms of cholera and of malarial poisoning may coexist, and so closely are they often associated that in many cases no distinction is made, and the mixed disease under the general name of fever is ascribed to malaria.

Fayrer says:

> With reference to the malarial origin of dysentery and cholera, I would remark that they seem closely linked etiologically, and that in some respects they present a closer resemblance to fevers than may at first sight appear, though they do not seem to be always under the same epidemic law of prevalence: witness the comparative statement of cholera and *fever* in Madras Presidency during the past seven years.[1]

Year.	Deaths from cholera.	Deaths from fevers.	Remarks.
1874..............	313	226,220	Shows that fever and cholera are not governed by the same epidemic laws.
1875..............	94,546	252,042	
1876..............	148,193	230,092	
1877..............	657,430	469,241	Famine year.
1878..............	47,167	374,443	Effect of famine still operating.
1879..............	13,296	285,477	" " "
1880..............	613	209,940	" " "

Colin says that in Cochin China, where the French troops suffered severely from cholera, more deaths also occurred from "choleraic pernicious fever" than from the other forms of pernicious intermittent—algid, etc.—although outside of the range of the choleraic influence this form is comparatively rare. The same fact was observed at Ancona in 1865, during which year a terrible epidemic of cholera raged in that city.

> At the moment when the Indian pestilence had almost entirely disappeared, there occurred still every day a certain number of grave attacks, which led to the belief that it was still present. These were pernicious fevers, which are far from being rare at Ancona, but which in this year, under the influence of the choleraic constitution, manifested themselves in this form with unusual frequency. The following year the cholera was at the gates of Civita Vecchia, among the workmen engaged in building a railroad upon the sea-shore, and I remarked here also the augmentation of the number of attacks of "choleraic pernicious fever" in our garrison in this city. It seems then that a special medical constitution favors the explosion of attacks of this kind, whether this constitution be based upon the influence of a cholera epidemic coming from India, or simply upon the elevation of the temperature, which in our country, and especially in England, causes to occur each year some cases of *cholera nostras*.[2]

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[1] Op. cit., p. 60.

[2] Op. cit., p. 253.

Comatose Pernicious Intermittent (*Congestive Fever*).

This is the most common form of pernicious intermittent, and almost the only form known in temperate regions. In the tropics also, the number of cases of this form is in excess of all other varieties of pernicious fever, if we exclude fevers due to the combined action of malaria and the specific poison of typhoid, yellow fever, or cholera. The attack may be sudden, "*apoplectic form*," and is frequently induced, in persons suffering from acute or chronic malarial poisoning, by the direct action of a secondary cause by which the enfeebled nervous centres—cerebro-spinal—are overpowered. Insolation, alcoholism, and excessive fatigue are the most potent exciting causes, and under the influence of one of these the patient may fall unconscious during a march, or while undergoing exertion of any kind. Or after exposure to the exciting cause he may, while asleep, fall into a state of coma, which is revealed to those around him by his stertorous breathing, or by his failing to awake at the usual hour in the morning. Upon attempting to arouse a patient in this condition it will be found that he can only be induced to respond to questions in monosyllables, and that he quickly falls again into a state of complete stupor after a momentary gleam of intelligence; or he may be completely unconscious, with dilated pupils, insensible to light, a pale face, a slow pulse, and labored respiration, which, according to Colin, does not become noisy in this form of malarial coma until after several hours, "at the moment when asphyxia commences from exudation into the bronchi."

The symptoms resemble those of serous apoplexy, and differ from those attending the coma which is developed during the hot stage of an intermittent paroxysm, or in a remittent attack, to be referred to presently.

Apoplectic malarial coma is more common in the autumn and among the victims of chronic malarial poisoning, while "congestive fever" attacks more frequently sthenic individuals, and especially unacclimated strangers, during the hottest season of the year.

The following case is reported by Colin:[1]

Tertian Intermittent Fever, Comatose Apoplectic Attack; Recovery.—Lecoz, *fusilier*, Eighty-fifth Infantry; admitted to the military hospital Saint-André, September 6, 1864. The patient has been stationed at the little town of d'Orte; he is yellow and meagre; liver and spleen enlarged; has had fever of tertian type, no paroxysm for four days. It is proposed to place him upon a reparatory regimen and to return him to his country for convalescence. September 15th, at the moment of our visit, he was found unconscious, paler than usual, lying upon his back in a state of complete inertia. The sensibility is so obtuse that we can scarcely arouse him by the application of a Mayor's hammer; respiration is slow, but unobstructed, the skin cool, the pulse 60.

The attendant had not even noticed the condition of the patient. He reports that the evening before, at eleven o'clock, the man had seemed for a few moments to be in a similar state of unconsciousness, but this symptom had disappeared before the arrival of the house physician.

We administered immediately a gramme of sulphate of quinine in solution, which was taken in our presence; a second dose of six decigrammes was administered an hour later; fifteen leeches were applied to the mastoid processes; sinapisms and aplications of Mayor's hammer to the legs and thighs.

At our evening visit the same day the symptoms persisted; another gramme of sulphate of quinine was administered, and two blisters were applied to the inside of the thighs.

September 16th, at the morning visit, the coma still persisted, and there had been no intermission since the last visit, but the sensibility is less obtuse; the patient tears the bandages from the blistered surface and seems to fix his attention when spoken to in a loud voice.

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[1] Op. cit., p. 238.

Prescription: Eight decigrammes of sulphate of quinine in a potion with ether, and a purgative enema. At the evening visit the coma had passed away, and the patient's face presented that mask of stupor which is so striking after a comatose attack. Improvement continued during the following days, and at the end of the month the patient was convalescent.

We remark that these cases of prolonged coma, not developed during an intermittent paroxysm, unattended with fever, and not periodic in character, are in our opinion more properly classed with the *sequelæ* of malarial toxæmia, than with the forms of disease due directly to the action of malaria.

The term "congestive intermittent fever," in the nomenclature employed in the reports of the Medical Department of the United States Army, includes all the varieties of pernicious intermittent heretofore referred to; but a majority of the cases occurring in the territorial limits to which these reports refer, no doubt correspond with the "*fièvre comateuse inflammatoire*"[1] of Colin, who says: "Of all the forms of pernicious fever, this, better than any other, may be considered as a symptomatic exaggeration of simple intermittent, and especially of simple remittent fever."

As in algid pernicious fever, the dangerous symptoms, unless directly induced by insolation, are commonly not developed until one or more paroxysms of simple intermittent have occurred; and not infrequently signs of approaching trouble may be observed in the intermission, or in the paroxysm preceding that in which these symptoms are developed. Sometimes there is severe headache and dizziness, or mental apathy and a disposition to drowsiness may be observed, with confusion of ideas and irritability of temper. The dangerous symptoms occur during the hot stage, when the febrile reaction is at its maximum, at which time the patient passes into a state of more or less profound coma. There may have been convulsions during the cold stage, although this is rare except in the case of children; and usually the beginning of the hot stage is attended with intense cephalalgia, which gives way as the patient becomes more and more disposed to somnolence and stupor. The face is flushed, the eyes often congested, the pupils wide and immovable (Hertz), the skin hot and dry. The respiration, at first irregular, becomes rapid and stertorous. The pulse becomes slow without losing its fulness, or may be rapid and small. At the outset of the attack there is cutaneous hyperesthesia, but this gives way to complete insensibility and the patient lies without feeling or movement, and not infrequently voids his urine involuntarily. Colin states that the only voluntary muscles in a state of contraction are those of the jaw, producing trismus.

The patient may remain in a condition of complete or partial coma for many hours, and when he finally regains consciousness, is more or less confused, exhausted, and apathetic. He is apt to complain of headache or dizziness, and very commonly is bathed in a profuse perspiration. Or the coma may continue and the case terminate fatally by a gradual failure of the heart's action and arrest of the respiratory movements. If the patient survives the first attack the next paroxysm is marked by the same symptoms in an aggravated form, unless it has been averted by prompt and vigorous treatment. A second attack is very likely to be fatal, and it is extremely rare that a third is recovered from.

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[1] "It must be understood that I attach to the expression 'inflammatory' no idea of organic inflammation. I give to this term the same signification as those who speak of the inflammatory period of yellow fever or of typhus, in order to express a more violent symptomatic and febrile movement, rather than a phlogosis" (op. cit., p. 230).

In these cases of congestive intermittent, coma is sometimes preceded by delirium, which occurs at the outset of the period of reaction—hot stage—and may be extremely violent. This symptom is more common, however, in the pernicious forms of remittent fever. The same may be said of epileptic or tetanic convulsive seizures, and we see no good reason for giving a separate account of "delirious pernicious fever," "convulsive pernicious fever," etc., etc., as some authors have done.

The following case of congestive (comatose) intermittent is reported by Colin:

Quotidian Intermittent Fever, becoming Comatose; Death.—Leclerc, *fusilier*, Nineteenth Infantry, admitted to the military hospital of Saint-André, August 27, 1864. Has been in Italy three years. Had previously been admitted to hospital with remittent fever. The present attack is a regular quotidian intermittent which has presented no unusual symptoms other than abundant epistaxis at the first three paroxysms. The fever yielded rapidly to sulphate of quinine, and after September 4th the patient, who had been out of bed each day, was put upon the régime of the convalescents.

September 13th, he experienced a very short chill toward ten o'clock in the morning, the hour at which his fever had previously occurred. There was no further development, and at three o'clock the same day, at the time of our afternoon visit, he took eight decigrammes of sulphate of quinine in our presence.

On the 14th, at the morning visit, the patient was free from fever and feeling well; at ten o'clock a very intense chill occurred, accompanied by lumbar pains and headache, which caused the patient to cry out; the hot stage commenced toward noon; the reaction was very intense, and was accompanied with great restlessness and incoherence of speech. At the moment when we saw the patient again (three o'clock in the afternoon) the skin was hot and moist (temperature 39.5° in the axilla), the face purple, the respiration noisy, the jaws locked, the muscles relaxed, the belly inflated; no vomiting or involuntary stools; cutaneous sensibility very feeble.

The epistaxes which the patient had suffered previously made us hesitate to apply leeches; by opening the jaws with a spoon we succeeded in administering fifteen decigrammes of quinine, a small part of which was rejected; two blisters were applied to the thighs.

Death occurred at nine o'clock in the evening. At the autopsy we verified the absolute integrity of the digestive tube; the spleen was reduced to a violet pulp (*bouillie*) of uniform tint; the same softening existed in two small supplementary spleens, the size of walnuts; the total weight of the spleen was two hundred and twenty grammes. The ventricles of the brain contained about forty grammes of serum; the cortical substance was of a deep ash-gray color and loaded with much pigment. This was also seen in the form of parallel blackish striæ in the tubular structure of the kidneys.

MORBID ANATOMY.—A fatal case of simple intermittent fever is almost unknown, and opportunities for post-mortem examinations in this form of malarial disease are consequently extremely rare. There is no reason, however, to suppose that the morbid lesions are different, except perhaps in degree, from those found in pernicious intermittent fever, and especially in the algid variety, which seems to be due entirely to the effects of malaria, while in the comatose form heat and other secondary causes play an important part in the production of the fatal symptoms.

When death is due to a complication or to an intercurrent malady, the morbid appearances will not be simply those induced by the malarial poison, and it will be necessary to exercise great care in an attempt to determine what lesions belong to the malarial disease and what to the complication.

Again, the fact that pernicious malarial fever, and especially the comatose variety, finds its victims in the tropics and during the hottest part of the year, makes it very necessary to be careful that post-mortem changes are not mistaken for morbid lesions resulting from the disease. It seems probable that this mistake has been frequently made. Thus Colin calls attention to the fact that the mucous membrane of the stomach and bowels quickly undergoes a post-morten staining, which has been taken for evidence of subacute inflammation. This author says: "That which proves that this is not the case, is that autopsies made in a cooler season of the year, and upon more debilitated subjects, no longer give these appearances of inflammation of the mucous membrane of the digestive tract."

The morbid anatomy will differ according as the subject has succumbed to a primary attack of pernicious intermittent, or to a congestive or algid paroxysm occurring in one already suffering from malarial cachexia as a result of repeated attacks of simple intermittent.

It would seem that if our object is to ascertain what are the primary lesions caused by the malarial poison, we should confine our attention to those fatal cases of acute malarial toxæmia known as algid pernicious fever, for in the complicated cases we are liable to fall into error, and in chronic cases we have to deal with secondary results, which, however interesting and important from a pathological point of view, throw but little light upon the main question, viz., the *modus operandi* of the malarial poison in producing the phenomena of the disease. It seems probable that the essential lesion, which clinical observations would lead us to seek in the nervous centres, has thus far escaped our researches, and that the morbid changes noted are to a great extent, if not altogether, secondary to changes in the living portion—the protoplasm—of the histological elements—nerve-cells—of the cerebro-spinal and sympathetic ganglia. We have no reason, however, to suppose that these changes by which the vital activity of a living nervous element is reduced or annihilated are demonstrable by the microscope, and in the absence of any such demonstration must content ourselves with recording the morbid lesions which are visible to the naked eye, or with the aid of the microscope. These are less marked in the quickly fatal pernicious fevers than in chronic malarial toxæmia, at least so far as organic lesions are concerned; the noticeable departures from a normal condition being usually nothing more than a certain amount of hyperæmia, with or without œdematous infiltration of the organs involved.

The changes in the *blood*, whether primary or secondary in their nature, are no doubt worthy of special attention. They have already been described at some length in Part First of the present volume. The leading fact in the pathology of the blood in intermittent fever, as well as in other forms of malarial disease, relates to the abundant destruction of the red corpuscles, and to the presence of black pigment, which is evidently derived directly from the coloring matter of the disintegrated corpuscles. This destruction of the corpuscles and formation of pigment occurs most extensively during a febrile paroxysm, and the corpuscular richness of the blood, at the time of a post-mortem examination, will therefore depend upon whether the subject has fallen a victim to a pernicious access while in a condition of robust health, or whether he has become anæmic from repeated attacks of simple intermittent. The pigment which is formed during an intermittent paroxysm does not, however, remain for any great length of time in the circulating fluid, and the amount found upon antemortem or post-mortem examination will doubtless depend partly upon the corpuscular richness of the blood of the individual, and still more upon the time which has elapsed since the seizure during which it was formed.

Aside from the presence of pigment there is nothing peculiar in the blood of patients dead from intermittent fever which can be recognized by the microscope. The red corpuscles are sometimes observed to be crenated, but this is frequently seen in the blood of patients dying from other acute febrile diseases; and in that of healthy individuals as well, under certain circumstances which relate not to the condition of the individual, but to the treatment which the blood receives while undergoing examination. The relative abundance of white corpuscles depends upon the degree of anæmia, and the blood of patients suffering from malarial anæmia presents no peculiarities by which it can be distinguished from that of anæmia from other causes, unless black pigment is present in it from a recent intermittent paroxysm. Colin says:

> During the years 1864 and 1865 I examined with the microscope the blood of nearly all the anæmics who, in autumn, were admitted to my wards. I expected to find in the blood an alteration corresponding with the splenic and cutaneous pigmentation, to verify the presence of pigment. Out of 65 cases in which I have noted the results of this examination I have only encountered pigment granules in three.[1]

Meigs has shown, however, that "pigment may exist abundantly in the visceral capillaries, and in the contents of the portal vein and other large vessels, when blood obtained from the derm and subcutaneous tissues does not exhibit it."[2]

The same author has noted that "in the acute stages of malarial fever, the red blood-corpuscles are darker than natural, appear soft, are sometimes crenated, readily yield their coloring matter when mingled with water, and are disposed to mass irregularly rather than to form distinct rouleaux."[3]

It is not claimed, however, that these appearances are *peculiar* to the blood of intermittent fever in its acute stages, nor could such a claim be sustained.

The physical characters of the blood—color, density, coagulability, etc.—will depend largely upon the *malarial history* of the patient. In sthenic individuals who have succumbed to an acute attack of congestive intermittent, these characters will not differ noticeably from those observed in other acute diseases; in anæmic subjects the blood will be found pale and watery, and coagulation will be imperfect. The difference among authors with reference to the amount of fibrine present, is doubtless due to this difference in the history of the patients examined. Léonard and Foley, who made a careful study of the blood of malarial fever in Algeria, found that while the albumen and red globules were reduced in quantity the fibrine varied but little from the normal amount.[4] Later observers have claimed that the amount of fibrine is also reduced, and there is no reason to doubt the correctness of their observations. Meigs, however, in a case of congestive fever found that the blood from the vena cava, "on standing separated into serum and *firm clot*, pinkish above, dark below."

The dark pigment formed in the blood is deposited in the various organs and tissues of the body, and especially in the spleen, the liver, the kidneys, the lymphatic glands, the brain, and spinal cord. It may also be demonstrated in the integument and in serous membranes, where it marks out the course of the blood-vessels, in the walls of which it is deposited. Some authors have been inclined to attribute to this pigment a very important rôle in the production of the morbid phenomena which characterize periodic fevers; and there can be little doubt that this insoluble granular material, which must be looked upon as a foreign element in the blood, is capable of giving rise to special symptoms, by blocking up capillary blood-vessels, and perhaps by acting as a mechanical irritant to the nervous centres. Interference with the function of the liver has been ascribed to the blocking up of the smaller branches of the portal vein, and icterus to an accumulation of pigment in the biliary ducts of small size (Grohe). The dangerous brain symptoms, such as coma, delirium, and convulsions, have also been explained in the same way, and it is very probable that this explanation is correct in certain cases. The capillary obstruction would naturally lead to serous effusion, or to extravasation of blood from rupture of the vessels. But this will not account for all the nervous phenomena, inasmuch as the amount of pigment found upon post-mortem examination bears no definite relation to the severity of these phenomena, which, moreover, are fully accounted for by the hyperæmia, œdema, and softening which may occur independently of the accumulation of pigment (Hertz). According to Heschl, the pigment is not found in the tissues of organs, but is deposited in the walls of the blood-vessels.

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[1] Op. cit., p. 398. [2] Op. cit., p. 110. [3] Ibid. [4] Colin, op. cit., p. 297.

The changes in the *spleen* in pernicious intermittent fever are said by Colin to be as constant and as characteristic as are the changes in the intestinal glands in abdominal typhus. These alterations consist in softening and pigmentation of the organ. The softening is less marked in the case of individuals who have succumbed at the end of a long series of intermittent attacks, in whom the spleen is often greatly hypertrophied and indurated. In these cases the unusual development of the fibrous framework of the organ gives it a certain amount of firmness, even when the parenchyma is softened.

Softening of the spleen is no doubt a very constant condition as a result of "pernicious fever," but it is not peculiar to cases of malarial origin. It is, however, extremely well marked in pernicious malarial fevers occurring in sthenic individuals in whom splenic hypertrophy has not been developed prior to the fatal attack. In these cases the spleen, when placed upon a table, may spread itself out "like a bladder half full of water" (Colin), the contents consisting of a dark-colored pulp, or of a black, bloody fluid. In most cases of pernicious intermittent a certain amount of hypertrophy also exists, and this may be very considerable—three or four times the normal size; but Colin states that in the absence of previous cachexia the organ does not usually attain the dimensions to which it arrives in typhoid fever. It is not uncommon to find discolorations and thickening of the capsule of the spleen and adhesions to neighboring organs. Infarctions also are not rare, and these may result in abscess or in gangrene. Rupture of the spleen attended with fatal hemorrhage may also occur (Hertz).

Pigmentation of the spleen, even when its parenchyma is diffluent, is said by Colin to be a characteristic feature which makes it possible to distinguish between the spleen of a victim of pernicious intermittent and the softened and dark-colored spleen of some other affections—*e.g.*, typhoid and scarlet fever.

We observe, on making a section, a general coloration, which varies from bright red to deep violet, and which in itself is in no way characteristic, but in the midst of this are little circular zones, of five to twenty-five millimetres in diameter, which at their circumference shade off into the general color of the organ, and which become gradually more deeply colored toward the centre, where they are black as coal.

Each of these zones corresponds with the section of a mass varying from the size of a pea to that of a small nut, and the number is in inverse proportion to the dimensions of these masses. When they are voluminous, they are very diffluent, and their surface is wrinkled by blowing gently upon it.

Microscopical examination shows that these masses are composed of the various elements of the blood, and especially by a great quantity of pigment, either in fragments with sharp and crystalline angles, or in granules more or less rounded or included in the leucocytes.[1]

In hypertrophy of the spleen from chronic malarial poisoning, especially when the immediate cause of death is not a pernicious febrile attack, the organ is unnaturally hard and friable, instead of being softened. This is due to an excessive development of the fibrous tissue of the capsule and trabeculæ of the organ, and in some cases to inflammatory exudates.

The capsule sometimes attains a thickness of two or three centimetres and is composed of several layers. According to Russell[2] the trabecular fibrous tissue does not increase with the increase of spleen pulp, and the malarially enlarged spleen is seldom met with of firm, tough consistence. This author asserts that:

> The permanent increase in bulk is mainly due to permanent increase in amount of spleen pulp, to a less degree, to the presence of exudative products of inflammation or congestion, as well as to more or less permanent dilatation of the arteries and increase in the amount of blood in the spleen.

Colin, on the other hand, says that hypertrophy is due to the excessive development of the fibro-muscular framework—blood-vessels and trabeculæ—of the organ, and that the splenic circulation is sometimes so much interfered with by the hypertrophy of the fibrous tissue that the organ presents a pale and lardaceous appearance. On section these spleens present white zones or patches of hypertrophied trabecular tissue alternating with slate-colored or marbled patches of pigmented parenchyma. In those cases in which, after being greatly enlarged, the spleen has again been reduced in size, it may be found atrophic, firm, and tough, with a large increase of its trabecular tissue, and almost entire disappearance of its pulp (Hertz). The extent of the enlargement varies greatly in different cases; often it is of enormous size, as much as fifteen or twenty times the normal size of the organ. Quain says that though in health it weighs only from five to seven ounces, in intermittent fever it attains a weight of eighteen to twenty pounds, and has been known to weigh forty pounds (Russell).

In fatal cases of pernicious intermittent the *liver* is found to be enlarged and hyperæmic, sometimes softened, and occasionally studded with apoplectic extravasations of blood. In chronic cases it is more or less enlarged and indurated from interstitial deposit; but, according to Colin, cirrhosis is of rare occurrence. Amyloid or fatty degeneration is found in certain cases, but there is no reason to believe that this is a direct result of the action of the malarial poison. Pigment similar to that found in the spleen is abundant in this organ, and upon section will be seen in the form of patches or striæ.

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[1] Colin, op. cit., p. 344.

[2] Malaria and Injuries of the Spleen, p. 59. Calcutta, 1880.

The *kidneys* also are usually hyperæmic and pigmented. The lesions characteristic of chronic Bright's disease and amyloid degeneration are sometimes observed, but these are secondary or accidental complications.

The *heart* in acute cases is found to be pale and flaccid, and sometimes presents evidence of fatty or granular degeneration. In chronic cases it is often enlarged, the cavities being dilated, and the walls in certain cases thickened. These changes are believed by Colin to be due to passive dilatation in the first instance, induced by excessive strain upon the organ during a series of intermittent paroxysms, and to a subsequent conservative hypertrophy of the cardiac muscle. In algid pernicious intermittent ecchymotic extravasations are often seen in the endocardium and pericardium, and the muscular structure may be dark, infiltrated, tender, and easily torn (Hertz). The right side of the heart is filled with dark blood, either fluid or imperfectly coagulated, as is also the vena cava and the large venous trunks generally.

The older authors laid much stress upon the changes in the gastro-intestinal mucous membrane. These were supposed to be of an inflammatory character, and induced Broussais to describe pernicious fevers under the name *gastro-céphalite*. Colin believes that post-mortem discoloration and softening has frequently been mistaken for evidence of subacute inflammation, and it seems very probable that this suspicion is well founded. Still there is evidence that in protracted cases hyperæmia, which is the characteristic lesion, may end in catarrhal inflammation. In complicated cases the pathological evidence of the complication will of course be found associated with those changes due to the malarial disease. Thus we may find evidence of a dysenteric complication in the large intestine, or of a typhoid or catarrhal complication in the small intestine, etc.

The *lungs* also give evidence of congestion ; the lower lobes are engorged, and in the algid form hemorrhagic infarctions are not infrequently encountered.

The lesions appertaining to the *nervous system* correspond with those found elsewhere, viz., hyperæmia with or without œdema, and occasionally hemorrhagic extravasations of small size, together with pigmentation. In sthenic individuals who have succumbed to a comatose pernicious paroxysm the brain is intensely hyperæmic, and a considerable amount of serum is found in the ventricles. The meninges are also injected, but present no evidence of inflammation. In the algid form the substance of the brain and cord is said to be pale, bloodless, dry, and tough (Hertz). This condition of affairs, however, indicates that the individual was in a cachectic condition when seized with the fatal paroxysm. Occasionally evidence of inflammation is found, when the pernicious attack has not been quickly fatal, but this is the exception, and should be considered a sequela or complication rather than a direct result of the malarial intoxication. The punctiform extravasations sometimes observed in the cerebral substance have been ascribed to blocking up of the capillaries by masses of pigment, but Heschl says they may exist independently of pigment formation, and that they are due to capillary aneurisms. Colin also believes that the pigment found in the minute hemorrhagic infarctions is a result and not a cause of the capillary blood stasis. This author does not accept the view that the pigment found in the various organs has been mainly formed in the spleen. He says :

> I am convinced that in place of coming from a distance, as emboli, the cerebral pigment is only a vestige of local congestion. In the spleen itself this material indi-

cates an exaggerated destruction of red corpuscles.[1] The same thing occurs in the brain, the liver, and the kidneys, in which the pigment indicates a destruction, entirely local, of the collections which occur during the violent sanguine congestion of these organs. In the same way we find, sometimes, in convalescents from typhoid fever, after resolution of the mesenteric glands, that these organs are deeply pigmented; that pigmentation of the large intestine is a vestige of dysenteric inflammation; that in old hemorrhagic foci in the brain we find blood pigment in all its forms (either in cells or in free crystals of hæmatoidine). In the same way the solid elements of the blood in pernicious fever undergo a dissolution, attested by similar results, in the principal organs in which it accumulates; only in this case the change will occur with a rapidity which is perhaps one of the most essential characters of this affection.

The following case of comatose pernicious fever is extremely valuable because of the full account of the morbid anatomy given by the distinguished author who has reported it—the lamented Dr. J. Forsyth Meigs, of Philadelphia:

CASE I. *Accumulation of Pigment in the Blood and Tissues—Pigmented Brain—Coma—Death.*—Unknown man, aged about seventy. Admitted Tuesday, October 13, 1865, 10 P.M. Taken ill upon a railroad train and brought to the hospital in a state of absolute unconsciousness, from which he could not be aroused. No further history could be obtained, except that he came from a Southern malarial district and had been suffering from fever. Pulse 105, feeble; skin dry; extremities cold, head and trunk warm; respirations frequent, loudly stertorous, jerky. Pupils very much contracted, uniform and symmetrical, not responding to light. No apparent paralysis of extremities, but fæces frequently and involuntarily voided. Dysphagia almost absolute.

Ordered: Hot bath, turpentine enema, blister to back of neck, one ounce of whiskey every hour.

October 14th, 11 A.M.—Has remained unconscious. Swallowed a portion of the whiskey. Skin warm throughout and moist. Pulse fuller, less frequent (92), very compressible. Pupils contracted ad minimum. Breathing as yesterday; tubes filled with frothy mucus; mouth filled with bright yellow fluid now vomited from the stomach.

Ordered: ℞. Magnesiæ sulph., ℥ ss.; olei tiglii, gtt. ij.; aquæ, q. s. M. Fiat haustus.
℞. Quiniæ sulph., gr. xij.; spt. frumenti, f ℥ j.; beef tea, f ℥ j.—M. S. q. h. per anum.

Blood (from finger). Red corpuscles dark, jelly-like, not crenated. Fine black pigment granules very abundant, free, and in cells presenting the appearance of white corpuscles. Rouleaux formed in masses. White cells increased in number, and large.

Died at 7.30 P.M.

Autopsy Four Hours after Death.—Body not emaciated. *Brain:* Of chocolate-gray color. On its section-surface the delicate tortuous vessels appeared abnormally distinct, and the white substance was throughout of a dull, dirty-gray hue. No conspicuous congestion of the vessels of convexity. Marked subarachnoid serous effusion over posterior superior part of convexity; also considerable fluid of the same character at base of brain. Shreds of lymph around the pons and anterior surface of cerebellum, and thickening of the membranes along the borders of Sylvian fissure. No apoplexy or ventricular effusion. *Spinal cord:* Leaden-gray on section. *Thorax:* Some pleuritic adhesions on left side. Very abundant pigmentary deposit in lungs; no tubercle; upper lobes crepitant throughout, but highly œdematous; lower lobes almost non-crepitant, but floated in water. *Heart:* Fibre firm; valves healthy, except small calcareous deposit on aortic surface of one semi-lunar valve; not sufficient to prevent its action. *Abdomen: Stomach* much distended; slightly congested internally. *Intestines* presented no glandular alteration; mucous membrane stained with bile; mesenteric glands slightly enlarged; numerous small points of pigment in the omentum. *Liver:* Edge thin, extending one inch below the sternum; dark olive-green on section. Gall-bladder moderately distended with dark bile, without calculi, and situated abnormally to the right of the transverse fissure, in a depression of the under surface of the right lobe. *Pancreas* healthy. *Spleen* very much enlarged, at least five times the size and weight of the healthy organ. Peritoneal investment irregularly thickened and whitish. At the anterior part of its upper extremity a thin film of blood-clot, firm, and evidently formed for some hours at least. The pulp was dark, of greenish tinge, and softer than is natural. *Kidneys:* Grayish-red, with dark points; firm; relative size of cortical and tubular portions normal. Cyst the size of a filbert-nut in the left, just beneath the peritoneum. Supra-renal capsules apparently healthy. *Blood* watery, depositing, on standing, black matter.

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[1] Two experimenters have succeeded in producing infarctions of the spleen in dogs and cats by section of the splenic plexus, characterized by the abundant presence of red corpuscles and by an enormous quantity of pigment in all its forms—diffused, crystallized, in cells, etc. (Jaschkowitz and Kowalewski, in Virchow's Archives).

Microscopic Appearances.—Blood from portal vein: Red corpuscles few, running together; no attempt at formation of rouleaux; darker than usual or very pale. White corpuscles much increased in number, varying in size, differently nucleated. Very many cells, similar to those of the splenic pulp and to those observed in blood from the finger, sometimes larger than ordinary white corpuscles, containing a great quantity of black granular pigment. Abundant free pigment grains and granules of various shapes and sizes; usually intensely black. *Blood from vena cava* (above junction of iliac but below renal veins): on standing separated into serum and firm clot, pinkish above, dark below. The lower layer contained red corpuscles running together as though almost diffluent; an increased number of white corpuscles; a few cells containing pigment granules, and some free pigment, but the grains smaller and fewer than in the blood of hepatic veins. Blood at base of brain contained numerous pigment masses. *Brain:* Capillaries of the white substance contained much granular pigment. Gray matter of a dark chocolate color; capillaries everywhere filled with pigment granules; a few pigment masses in the tissue substance proper. *Spinal cord:* A collection of pigment granules in all the capillaries. *Spleen:* Pulp containing red blood-corpuscles; connective-tissue cells; many cells with granular pigment and others without it; free black grains and granules throughout in large quantity. *Heart:* Muscular fibre healthy; capillaries containing pigment; large black masses and granules free in the tissue. *Mesenteric glands:* Firm, somewhat enlarged. Section-surface exhibited a dark ring near exterior of gland, seen under a lens to be due to abundant pigment entangled in the gland structure. *Liver:* Cells with nuclei as in health; much pigment in masses and granules, adhering to the cells or existing within them—*i.e.*, in their "formed matter." In the blood of hepatic vein, pigment cells such as seen in portal vein and spleen. The omentum was dotted with small black points of pigment entangled in the fibrous tissue. *Kidney:* Malpighian tufts dotted with pigment; free masses in the renal tissue. Epithelium healthy. *Urine:* Acid; a few granular casts, vesical epithelium, and numerous spermatozoa; no albumen; no pigment.

REMARKS.—I had never before seen a brain presenting such an appearance. It was leaden-colored throughout, as long ago described by Morgagni, who is quoted by Frerichs. The hue of the gray matter was most singular. It looked as though it had been washed over with a not very weak solution of India-ink. I examined many specimens with the microscope. In every one of these all of the capillaries were unusually distinct, and were crowded with black pigment in the form of granules, lying in their calibre or deposited apparently in the walls themselves. There existed also, scattered through the cortical brain-substance, isolated grains of pigment much too large to be embraced in a capillary tube. It was evident that the general dark color of the cerebral tissue and substance of the spinal cord was due to this aggregation of minute grains and granules. Wherever the blood had gone it had taken the pigment, filling the capillaries and lodging it in the tissues. To the naked eye, and more particularly to the eye aided by a pocket lens, the fine vessels of the white medullary matter were everywhere visible, resembling, as Dr. Bright aptly remarks, the "appearance produced by scraping the nap of fine cloth upon a sheet of white paper." The color of the liver was olive-green, as stated in the notes. The term "bronzed liver," employed by Dr. Thomas Stewardson in his paper on "Bilious Fever," already referred to, most correctly expresses this appearance. I was resident physician in the hospital at the time Dr. Stewardson's observations were made, and I well recollect the appearances as seen. They were the same as regards the liver as those present in this instance. The case above described is strikingly similar to that detailed by Bright and to those classified by Frerichs under the head of "cases with cerebral disturbance." Not only were the post-mortem appearances of the blood and tissues entirely analogous, but, as in many of the instances cited, the patient first came under notice in a state of unconsciousness; the series of pathological conditions having ended (probably during a febrile paroxysm) in the *sudden* occurrence of convulsions, stupor, coma, and early death.[1]

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[1] Sometimes severe brain symptoms, which speedily prove fatal, are developed after only a few hours of vague indisposition without any distinct febrile symptoms manifesting themselves. In other cases a simple intermittent fever has existed for weeks or months when suddenly a severe fit comes on which often terminates fatally in an instant (Frerichs, vol. i., p. 332).

TREATMENT.—Physicians as a rule give but little attention to the treatment of the febrile paroxysms in simple intermittent, inasmuch as they are not attended with any danger to the patient and because the main indication is evidently to prevent the periodic return of these paroxysms by specific medication. The treatment of the "ague fit," therefore, for the most part, comes within the province of domestic practice. Its object is to alleviate, as far as possible, the uncomfortable sensations of the patient during the cold and the hot stages of the paroxysms and to encourage cutaneous transudation, as the inauguration of the sweating stage is attended with an alleviation of the fever, headache, and other nervous symptoms.

In the comparatively brief paroxysms of the tertian and quartan type the physician may safely leave the patient to his own resources or to those of his immediate attendants. But in the more protracted paroxysms of the quotidian type he will frequently be called upon to prescribe for the relief of distressing symptoms connected with the febrile attack, and in the *pernicious* forms the life of the patient will often depend upon his prompt and judicious interference.

Treatment during the Paroxysm.—The sensations of the patient during the cold stage seem to furnish an indication for treatment; but it must be remembered that these sensations are of nervous origin, and that while his teeth are chattering and he complains of being very cold, the temperature of his blood is already above the normal, and that these chills occur most commonly during the warm season of the year, and often when the external temperature approaches that of the human body in health. Under these circumstances, to cover the patient heavily with bedding or to administer hot drinks is productive of harm rather than good, as the interior body-heat is increased, without any relief to the condition upon which the rigor depends or to the chilly sensations of the patient. The body should be lightly covered, however, and the patient protected from currents of air. The *external* application of heat is a very different matter, and is decidedly useful. Reaction is encouraged and the patient commonly experiences great comfort from such applications, which may be made in the form of pediluvia, or by means of bottles or "rubber bags" filled with hot water, hot bricks, etc. Remedies which act directly upon the nervous centres are far more potent for the relief of rigor, and by these not only the cold stage but the entire paroxysm may be very much abridged and the distressing symptoms alleviated. One of the most useful of these remedies is *opium*, which, according to Dr. Wood, "often affords great relief, and sometimes shortens the chill and moderates the subsequent fever."[1] The following testimony relating to the beneficial action of this drug is given by Dr. James Lind:[2]

Having given a dose of opium in an obstinate case of ague, on account of some accidental symptom, to the great relief of the patient, Dr. Lind decided to give the remedy a more extended trial, and it was administered to twenty-five patients, immediately after the hot fit, with benefit so far as the relief of headache and other nervous symptoms was concerned.

> Encouraged by this success, I next day ordered the opiate to be given during the hot fit. In eleven patients out of twelve to whom it was thus administered it removed the headache, abated the fever, and produced a profuse sweat, which was soon followed by a perfect intermission. Since that time I have prescribed an opiate to upward of three hundred patients laboring under the disease. I observed that when

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[1] Op. cit., vol. i., p. 265.

[2] Lind on Hot Climates, Phil. ed., p. 236 (quoted from Bartlett, op. cit., p. 393).

given during the intermission it had not any effect, either in preventing or mitigating the succeeding fit; when given in the cold fit it once or twice seemed to remove it; when given half an hour after the commencement of the hot fit it generally gave immediate relief.

The effects of opium given in the hot fit of an intermitting fever are three: First, it shortens and abates the fit, and this with more certainty than an ounce of bark is found to remove the disease. Second, it generally gives a sensible relief to the head, takes off the burning heat of the fever, and occasions a profuse sweat. This sweat is attended with an agreeable softness of the skin instead of the disagreeable burning sensation which usually affects patients sweating in the hot fit, and is more copious than in those who are not under the influence of opium. Third, it often produces a soft, refreshing sleep, to patients before harassed with fever, from which they awake bathed in sweat and in a great measure free from complaint.

I have always observed that the effects of opium are more uniform and constant in intermitting fevers than in most other diseases, and are then more quick and sensible than most other medicines. An opiate thus given soon after the commencement of the hot fit, by abating the violence and lessening the duration of the fever, preserves the constitution uninjured. Since I have used opium in agues, a dropsy or jaundice has seldom attacked any of my patients in these diseases.

Fayrer says: "The antiperiodic powers of opium are probably the chief reason why opium-eating and smoking has become so widely spread a habit in China and India." There may be some question as regards this; but, if it be true, no one in this country would think of administering the drug as an antiperiodic, and it is only because of its recognized value in arresting or mitigating the distressing symptoms of the febrile paroxysm that attention is called to it in the present place. Waring says that he has seen opium act like a charm in abridging the cold stage and in mitigating the severity of the hot stage. Colin says that opiates administered at the outset of an attack not only quiet the nervous excitement, but also diminish the duration of the paroxysm. Notwithstanding this evidence in their favor, we do not recommed a habitual resort to opiates during the paroxysms of intermittent, and would reserve this remedy for exceptional cases, and especially for those in which the nervous symptoms are unusually severe and the patient poorly fitted to endure them. No doubt in properly selected cases the administration, by hypodermic injection, of one-eighth to one-fourth of a grain of morphia will be attended with the happiest results so far as the immediate relief of the distressing symptoms is concerned.

Another remedy which often cuts short the stage of chill and abridges more or less the febrile stage is *chloroform*, administered internally in drachm doses. The value of chloroform administered in this manner has been insisted upon by several authors, and especially by Merrill,[1] McClellan,[2] Eagan,[3] and Scott.[4]

Dr. Eagan says:

In order to obtain the full measure of its therapeutic influence, chloroform should be given, as insisted upon by Dr. Merrill, in "physiological doses" of f. ʒ j., to be repeated at the interval of fifteen minutes or half an hour till its full hypnotic effect is experienced. Employed in this way it will, in a large proportion of cases, arrest the paroxysm in the first stadium, and when it fails to do so it will almost invariably diminish its intensity and to that extent lessen the severity of the succeeding hot stage.

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[1] The discovery of the value of chloroform internally administered in the cold stage of fever is said by Eagan to have been made by Prof. A. P. Merrill, of New York, in 1852.

[2] Surgeon Ely McClellan, U.S.A , in Am. J. of the Med. Sc., Phila., July, 1866, pp. 271-4.

[3] Dr. Samson Eagan, Jefferson City, Texas, N. Orl. M. & S. J., Oct., 1868, p. 701.

[4] Dr. D. Scott, of Bellefontaine, Iowa.

> We have employed the remedy largely in this condition for the last eight years in the manner above specified, and we take pleasure in offering our feeble testimony as to its perfect safety and efficiency in bringing about reaction from the cold stage of fever beyond all other remedies with which we are acquainted. . . . The immense value of this agent can be duly estimated only by witnessing its operation in the cold stage of a pernicious paroxysm in cases in which the patient is seen too late for the great antiperiodic quinia to be available. . . . . Perhaps in no other pathological condition is the curative power of medicine exemplified in a manner more positive and striking.[1]

Dr. Scott's testimony is as follows:

> In twenty cases, after the administration of one fluidrachm each, the chill was immediately arrested, with the exception of one case, in which the above dose was repeated in one hour; in eleven of the above cases the febrile stage was probably abridged; in the remaining cases the fever ran about as usual, all, with few exceptions, terminating in profuse perspiration; in eight of the cases the paroxysm returned on the succeeding day, in nine on the second day, and three escaped, but were subsequently attacked in from seven to twenty days; in the remaining cases, no reliance was placed on the curative properties of the cholroform (which I only administered for the purpose of abridging the chill), which was followed by large doses of sulph. quiniæ as soon as the sweating stage was established.—In conclusion Dr. S., says that chloroform is a valuable and safe hypnotic in the dose of one fluidrachm, in the cold stage of intermittent fever, and never fails to arrest the chill, the patient falling into a refreshing slumber as described by Dr. McClellan. Dr. S. administered it, like Dr. McClellan, undiluted.[2]

The inhalation of chloroform, of cinchonic ether, ʒ j. (Groh), and of amyl nitrite, gtt. 2 to 3 (Saunders), has also been recommended for the abortion of the paroxysm, or at least of the cold stage, and no doubt all of these remedies have a certain value.

Various other methods have been recommended for the same purpose. Thus Von den Broch[3] claims to have prevented the development of a paroxysm in 60 out of 89 cases, in the military hospital at Mons, by the use of hot mustard foot-baths, half an hour before the expected return of the fever; Audouard[4] recommended large sinapisms, applied to the limbs immediately before the attack; Lallour[5] has claimed that general friction with camphorated alcohol will abort the paroxysm; Gondret[6] reports great success from the use of numerous dry cups, applied along the spine; Bailly[7] recommended ligature of the extremities, and general and methodical compression of the abdominal cavity to diminish the amount of blood in this cavity; Surgeon Kennedy,[8] of the Confederate Army, discovered that the return might sometimes be prevented by applying a bandage wet with turpentine around the body at the lower part of the chest, half an hour before the expected paroxysm.

When the chill is severe and protracted, Dr. George B. Wood recommends the hot vapor bath, which may be given by raising the bedclothes over the patient by means of crossed half-hoops, and placing near the body hot bricks wrapped in wet flannel. The same author advises the use of hot drinks, such as lemonade, toast-water, or infusion of balm. Warm drinks are commonly used in this country in domestic practice, and are also recommended by Fayrer, Colin, and others. Hertz, however, is opposed to their use.

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[1] Op. cit., p. 701.

[2] Am. J. of the M. Sc., Phila., April, 1868, p. 562.

[3] Bulletin gén. de thérapeutique, 1855.

[4] Nouvelle thérapeutique des fièvres int. Paris, 1812.

[5] Thèses de Paris, 1856.

[6] Bull. de l'Acad. de Méd., t. xv., 688. 1858.

[7] Traité des fièvres int., p. 446.

[8] Confederate Med. and Surg. J., No. 1.

In the algid form of pernicious intermittent fever the indication seems to be still more pronounced for the external application of heat, and of revulsive remedies, such as mustard, turpentine, red pepper, etc., and experienced practitioners in all parts of the world are in accord as to the propriety of resorting to these measures, which, however, all agree are often quite inadequate to bring about the desired reaction, which is more surely induced by remedies acting directly upon the nervous centres, and especially by the sovereign remedy, quinine. Some physicians have thought it necessary to apply blisters to the thighs and elsewhere in these algid paroxysms, but this practice is only mentioned here for the purpose of condemning it. It is doubtful whether the revulsive effect of the blister is equal to that of large sinapisms moved from place to place, and it is certainly taking an undue advantage of the helpless condition of the patient to inflict upon him the suffering which he is sure to experience from the blistered surface, if he is fortunate enough to survive the pernicious attack.

The internal use of stimulants is not to be recommended in these cases. We believe that the general experience of the profession is in accord with that of Davidson in this particular, who says, "My own experience has been that stimulants, as a general rule, are not well borne by the stomach, but increase vomiting, and are apt to prove injurious when reaction takes place."[1]

A mode of treatment quite the opposite of that heretofore referred to has been recommended for the prevention of an approaching paroxysm, and for the relief of the algid condition in pernicious intermittent fever. This consists in the use of cold water in the form of a bath or douche. The value of this method of treatment, especially in comatose and in algid pernicious paroxysms, is beyond question, and has the endorsement of some of the highest authorities in our own country and abroad.

Truka[2] advised the use of the cold bath in advance of the expected return of an intermittent paroxysm, as an abortive measure. Currie[3] also resorted to cold affusions an hour before the invasion of the initial chill, with the view of preventing the attack. Others have resorted to the use of cold baths, wet packs, etc., only during the hot stage, and with the view of modifying the intensity of the febrile movement and its duration.

But it is especially in pernicious fevers that this remedy has given the most striking and beneficial results, and next to the administration of the sulphate of quinine in large doses, it is probably our most valuable resource in these cases. It may seem a bold experiment to dash cold water over a patient who is almost, or entirely, pulseless, whose extremities are cold to the touch, whose lips are livid or bloodless, and whose features are pinched and shrunken; but the experiment has been frequently made with the most happy results. Dr. George B. Wood says:

> Some practitioners in the West and Southwest habitually employ cold affusion or the cold bath (as a means of producing reaction). Dr. Gustine, of Natchez, informed the author that he had once immersed a patient, while in the lowest stage of a pernicious paroxysm, with a cold skin, and nearly or quite pulseless, but complaining bitterly of the burning heat which was consuming him, in a bath of cold water, with the happiest effect. The remedy was agreeable to the patient, and he was allowed to remain until he began to feel somewhat chilly, when he was removed, wiped dry, and placed in bed. Reaction soon came on delightfully, and his life was saved.[4]

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[1] N. Orl. Med. & Surg. J., Feb., 1880, p. 755.

[2] Historia febrium intermittentium. Vienna, 1775.

[3] Medical Reports on the Effects of Water, Cold and Warm, etc. Liverpool, 1793.

[4] Practice of Medicine, vol. i., p. 315.

Other evidence of the same kind is given by this author, who judiciously remarks that "Nature seems to point to the remedy by the burning heat of which the patient complains, and the great comfort he derives from the application. Nor is it irrational. The nervous system is chiefly in fault in these cases. A strong impression is made upon that system by the sudden application of cold to the skin. If there be any power of reaction left, it is apt to be awakened by this shock." In the application of the remedy in the algid condition, it must be remembered that it is not abstraction of heat that is required, but a strong impression upon the nervous centres. The proper method of application and the favorable effect produced by the cold douche in these cases is well shown by the following case, reported by Davidson:

Mr. J. N——, a planter, of middle age, robust in form and of general good health, was attacked, in the month of October, with a tertian intermittent fever, and was attended by Dr. L., a physician of standing and long experience in the profession. The paroxysms were marked by no special indications of any tendency to a pernicious form, beyond the continuance, during the periods of intermission, of some degree of restlessness and nausea. His physician had applied wet cups to the epigastrium, gave the patient calomel, and administered quinia in full doses during the apyrexia.

In the third paroxysm, which took place early in the forenoon, the patient passed suddenly into a collapsed state, and about three o'clock P.M. I was called to see him in consultation. I found him in a calm frame of mind, suffering no acute pain, but complaining of a sense of oppression and stricture about the chest; the respiration was frequent, with a double effort at inspiration. He complained of nausea and heartburn, attended with a feeling of great internal heat, accompanied with intense thirst. The pulse was threadlike, rapid and hardly perceptible at the wrist; eyes sunken, voice puerile, skin bedewed with a cold, clammy sweat; the extremities very cold, the skin about the ears, back of the neck, and the extremities of a purplish, livid hue, and the integuments of the hands and fingers wrinkled as if they had been in water. The jactitation was very great, and the bowels running off, the stools being copious and liquid; the tongue was coated with a thick white fur, pale and broad. The surface of the chest and abdomen was warm. Under the perverted nervous condition characteristic of this collapsed state, all warmth applied to the cold surface was unpleasant, and the patient complained even of the heat of the hand when applied to the pulse.

Informed by his physican of the almost hopeless nature of his case, he had summoned his pastor, a Presbyterian minister, who was at his bedside when I entered the room. I determined to use the cold douche, to which Dr. L. consented, the patient being left in my charge while the doctor visited his family. It was practised in this way.

The patient, perfectly nude, was laid supine on a blanket stretched upon the floor. A large tub of very cold water, procured from an abundant and shaded spring, was provided, and standing at his head, I threw a large bucketful of water with considerable force from his chest downward. The shock was severe but not unpleasant, as he afterward informed me. Four bucketfuls in rapid succession were thus applied, and the patient replaced in bed upon a sheet, and thoroughly rubbed dry, after which the sheet was removed and blankets placed over him. An enema containing sixty grains of quinine, forty drops of laudanum, and an ounce of brandy, in four ounces of thin starch water, was thrown into the bowels, and a compress held to the person to assist in its retention. Bottles of hot water were applied to the feet, and the whole surface of the body and extremities was rubbed briskly with dry mustard. Brandy toddy was administered in small draughts, but was discontinued, as it gave rise to a burning sensation in the stomach and brought on nausea.

The immediate effect of the douche was evinced in diminishing the frequency and irregularity of the respiration, allaying the thirst and jactitation, and temporarily raising the pulse, which could be felt somewhat more distinctly at the wrist.

The enema was passed in about forty minutes with a considerable thin dejection. Shortly afterward all the restlessness and disquiet returned, with the previous interrupted and hurried respiration.

The douche was again resorted to, the patient himself anxiously calling for it, and desiring that he should receive it in a prone position. Four more bucketfuls of water were dashed upon him, and, when replaced in bed, the enema, with sixty grains of quinine, sixty drops of laudanum, and one ounce of brandy, was at once given, and the dry heat to the extremities and frictions repeated as before.

The reaction was somewhat more marked after this douche, the patient expressing decided relief from the sense of internal heat, the respiration becoming slower and more regular, and the pulse could be felt distinctly enough to be counted, with some feeling of returning power. Though some retching occasionally took place, no vomiting occurred, but the patient spat off quite frequently a white frothy mucus

At the expiration of two hours, notwithstanding the persistent use of frictions to the extremities, and with turpentine along the course of the spine, and a cautious repetition of the brandy toddy, what was gained by the last douche seemed to be disappearing.

It was again repeated and carried to the same extent and in the same posture. The enema having been retained, it was deemed best to repeat the quinia in the same dose and with the adjuvants before named, care being taken to have it retained. Heat was applied to the extremities and the frictions were continued. Not long afterward the patient fell into a calm sleep, which lasted a short time.

Reaction steadily progressed, the pulse developing and the heat of the trunk gradually extending to the extremities. From this time forth all the untoward symptoms, little by little, passed away, and the escape of the patient from the peril in which he had been so suddenly plunged, was assured.

The reaction became full and complete, and the patient, throughout the next day, was able to take appropriate nourishment and to retain several doses of quinia, ten grains being given at intervals of three and four hours to keep up cinchonism and prevent another paroxysm. No further medication was needed in the case beyond a dose of oil to move the bowels some days afterward.

Dr. Davidson, after narrating this instructive case, remarks: "The cold douche should not be indiscriminately practised, and should be restricted to persons of a sufficiently robust constitution to bear the shock, and whose vital powers have not been exhausted by long continuance of malarial or other disease. In a modified form, however, it could be beneficially used in many cases with whom the douche would be deemed hazardous."

This method of treating the algid condition in pernicious fever has the high endorsement of Prof. N. S. Davis, of Chicago, who recommends that the patient be stripped and several gallons of cold water dashed suddenly over his head and body, after which he is to be quickly rolled up in dry flannel blankets for thirty minutes. If there is no decided improvement at the end of this time the cold douche is repeated, and he is again wrapped in warm blankets.

In comatose cases, attended with a high temperature, the use of cold water is still more strongly indicated. It should be used in these cases, when the head is hot and the face flushed, as a local sedative, an ice-cap being applied to the head and back of the neck (Davis); and also to reduce the body heat by means of the cold bath, wet pack, or sponging. When the comatose condition is attended with symptoms of collapse, the shock produced by pouring cool or tepid water upon the head, face, and thorax, from an elevation of several feet, will be found more efficient in relieving the oppressed brain, than is the continuous application of cold to the head. At the same time it will be necessary to resort to the use of rubefacients and dry heat to the extremities. In choleraic cases Davis says[1] that much benefit may be derived from the use of morphia and atropia administered hypodermically, and if the heart's action is very feeble he would give alternately with these, suitable doses of strychnia. In purely algid cases the same author advises the use of strychnia and atropia, without morphia, either administered hypodermically or by the stomach.

The temptation will be strong in these cases to administer stimulants internally, but experience has amply demonstrated that alcoholic stimulants are commonly worse than useless. This was the opinion of Drake, and is that of Davis, of Davidson, and of those practitioners in our own country, generally, whose experience enables them to speak with authority. It will be understood, however, that reference is here had to the inutility of alcoholic stimulants for the relief of the algid condition, and does not apply to those conditions of partial collapse which depend alone upon failure of the vital powers, and which occur especially in aged and feeble persons, as a result of a severe paroxysm of intermittent. In these cases alcoholic stimulants are decidedly useful and often indispensable. Other stimulants, more prompt in their action, such as ether, camphor, or carbonate of ammonia, may also be required for the relief of threatened syncope. An excellent substitute for alcoholic stimulants will often be found in a cup of black coffee, which may be given by enema if the stomach is irritable and not likely to retain it.

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[1] Boston Medical and Surgical Journal, March 3, 1881

When the chill is attended or preceded by nausea, and by ineffectual efforts to vomit, it is best to administer at once a prompt emetic. For this purpose a teaspoonful of powdered mustard diffused in warm water is a favorite prescription, especially in domestic practice ; or an emetic dose of ipecacuanha may be given. In case of irritability of the stomach with frequent vomiting of acrid, sour, or bilious matter, Wood recommends a copious draught of warm water to wash out the stomach, and if this does not give relief a sinapism to the epigastrium and an anodyne enema.

When reaction is fairly established the patient will require cooling drinks ; and those remedies which have a tendency to moderate the febrile movement and to produce diaphoresis may be prescribed. Dr. Wood's favorite prescription, the effervescing draught, is no doubt of value at this time. It is said to soothe the stomach, to diminish fever, promote perspiration, and favor a solution of the paroxysm.

The popular idea that the rapid fall of temperature, which commonly occurs during the sweating stage, is *due* to the profuse perspiration, is not justified by the results of exact observation. For Ringer has shown that the temperature may continue to rise while the patient is bathed in perspiration, artificially induced. He says :

> I will now adduce additional evidence to show how little share the dry skin plays in the production of the febrile temperature. Two patients were admitted under my care with ague. I determined to excite profuse perspiration before, or just before, the commencement of the febrile paroxysm, and to watch what effect this free perspiration might have on the high temperature. The first patient suffered from quotidian ague, and his temperature rose in an untreated paroxysm to 105° and 106° F. Just before the onset of an attack, I gave him half a grain of pilocarpine, which in twenty minutes produced copious perspiration ; yet, in spite of this, the temperature rose six degrees, to 104.4°, and the fit lasted as long as on previous days, the temperature falling short of the attacks on the previous days by about a degree. As in ague the untreated fits often differ to a greater degree than this, it is doubtful if even this slight diminution was due to the jaborandi. I may mention that the sweating produced by the jaborandi had very little influence on the shivering, and blueness of the lips, nose, and extremities.
>
> The next patient suffered from irregular tertian fever caught in Florida. In an untreated attack, on August 1st, his temperature rose to 104.8°. On August 4th the rigor began at 3.20 P.M., his temperature at that time standing at 101° F., conforming to the rule with ague, that the temperature rises one or two degrees before the rigor begins. Five minutes after the beginning of the rigor, Mr. Neale, my resident assistant, administered hypodermically a quarter of a grain of pilocarpine. In a quarter of an hour perspiration began, the temperature standing at this time at 102.6°. The perspiration soon became profuse, and yet at 4.30, fifty minutes after the commencement of free perspiration, the temperature stood at 105.5°, and continued above 105° till 5.30 P.M., when the fever began to decline, and the temperature became normal between 1 and 3 A.M. on the following morning, the fit lasting more than ten hours. On August

> 7th he had a fit which was untreated. On August 10th he had another attack. At 3.20 his temperature was 101.8°. At 3.30 Mr. Neale gave him a hypodermic injection containing half a grain of pilocarpine. At 3.45 he was perspiring very freely, and his temperature marked 102.1°. At 5.30 the temperature was 105°, and subsequently rose to 105.2°. It remained at or above 105° till 8 P.M., and then fell, becoming normal at 4 the following morning; the fit, therefore, lasted over twelve hours. On August 13th he had another attack. At 5 P.M. his temperature was 101°. At 5.30 half a grain of pilocarpine was administered hypodermically. At 5.45 he was sweating, and his temperature then marked 103°. At 7.15 his temperature stood at 105.4°, and so remained till 8 P.M., and after this time it fell, becoming normal between 3 and 5 the following morning. In this case the attack lasted more than ten hours.
>
> In these experiments, then, the temperature in an untreated attack rose to 104.8°. In the three fits treated with pilocarpine, which produced copious perspiration, the temperature reached respectively 105.6°, 105.2°, and 105.4°, the fits lasting, respectively, ten, twelve, and ten hours. We may therefore fairly conclude that the free perspiration had a very insignificant influence on the febrile temperature, and the increased heat cannot be explained by its accumulation owing to a dry skin, but must be due to increased production of heat from increased combustion.[1]

The writer has seen the same thing occur in yellow fever, in cases in which, by the use of numerous blankets and hot drinks, a profuse perspiration had been produced with a view to "breaking the fever." The temperature under such treatment may mount to a dangerous point, while the patient's bedding is saturated and his body bedewed with perspiration.

On the other hand, certain remedies reduce temperature, by their action upon the nervous centres, without producing perspiration. Aconite is a remedy of this class, as has been shown by Ringer in the valuable paper from which we have just quoted. This may be given alone or in combination with a mild diaphoretic or diuretic medicine. A favorite prescription with the writer is the following:

℞.	Tr. aconite r.	gtt. x.
	Spts. ætheris nit.	℥ss.
	Aquæ.	℥iijss.

M. Sig.—A tablespoonful every hour.

When the object in view is to effect a speedy reduction of an excessive and threatening degree of pyrexia, the cold bath or wet pack will be found the most efficient remedy, or a full sedative dose of quinine may be given. The hesitation formerly entertained with reference to the administration of this remedy during the hot stage of malarial fevers has been shown to be without foundation, especially when a full sedative dose (30 grains for an adult) is given. Small doses, however, often increase the headache and nervous symptoms without doing any immediate good. The application of evaporating lotions, of cold water, or even of an ice-cap, to the head, will be indicated whenever there is severe headache or a tendency to coma. Nervous symptoms not depending upon excessive pyretic action or cerebral congestion may often be relieved by the administration of potassium bromide in full doses.

Cases may occasionally occur, in sthenic individuals, in which the abstraction of blood by venesection, by leeches, or by wet cups will be justifiable and perhaps imperative; but these cases are likely to be extremely rare, and it is only in comatose cases, occurring in full-blooded individuals who have recently arrived in a malarial region in southern latitudes, that we would consider this a necessary measure for the immediate relief of the dangerous symptoms.

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[1] Sydney Ringer in Braithwaite's Retrospect, January, 1879, Part lxviii., p. 51 (Abstract).

The *sweating stage* of an intermittent paroxysm requires no special treatment; commonly the patient is disposed to sleep, and he should be lightly covered up in bed, protected from draughts, and left quiet. If exhausted by the severity and duration of the paroxysm a stimulant may be required, or he may have a cup of black coffee.

In *pernicious* paroxysms which threaten life, in addition to the remedies heretofore mentioned, it is necessary to resort *at once* to the administration of full doses of sulphate of quinine. This may be given by the mouth, by enema, or by hypodermic injection. The object should be to obtain the full physiological effects of the drug as soon as possible, and not to give more than is necessary to accomplish this purpose. Twenty grains, dissolved by means of aromatic sulphuric acid, may be given at once, and repeated in two or three hours, if necessary, or, if the symptoms are urgent, thirty or forty grains may be given at first. As an enema, forty grains, combined with thirty drops of laudanum would be a proper dose. But in cases where from inability to swallow, or irritability of the stomach, the medicine cannot be administered by the mouth, it will be best to resort at once to the use of the hypodermic syringe. The dose will be from five to ten grains, to be repeated in an hour or two if necessary.

SPECIFIC TREATMENT OF INTERMITTENT FEVER.—In all parts of the world where malarial fevers are prevalent, it is now generally recognized that quinine is entitled to the first place in the list of remedies for these diseases, and that it is, *par excellence*, the specific against malarial poisoning—we cannot say the antidote to malaria, for it is not definitely settled whether quinine neutralizes the poison or its effects upon the system, although the weight of evidence seems in favor of the latter view (see p. 110). The great French clinical teacher, Trousseau, says: "It is generally believed that cinchona and its substitutes are in all cases the antidotes of the morbid cause; that they neutralize the cause, as mercury is believed to neutralize the cause of syphilis. It does not seem to us to be exactly thus. Cinchona often lets the cause remain in all its intensity, but puts the system in the state for resisting it."[1]

It is mainly in localities where malarial diseases, properly so called, are little known, and where pseudo-malarial fevers prevail, as in some of our northern cities, that we find physicians complaining of the failure of quinine to cure "malaria."

Nevertheless, it must be admitted that persons constantly exposed to malarial influences, and who have repeatedly resorted to the use of quinine in large doses, seem to acquire a certain tolerance to its action, and that in such cases its specific virtues sometimes fail to manifest themselves. It will often be found, however, that in these cases the administration of exceptionally large doses will produce the physiological effects of the drug, and arrest the progress of an obstinate intermittent fever. Persons suffering from malarial poisoning have a greater tolerance for quinine than have those in health, and this tolerance seems to bear a direct relation to the intensity and duration of the symptoms of malarial toxæmia. The dose, therefore, must be proportioned to the severity of the symptoms. Thus a dose which would quickly cure a first attack of simple intermittent in a sthenic individual, would be entirely inadequate to prevent the return of a pernicious paroxysm in one already suffering from malarial cachexia.

In ordinary cases fifteen to twenty grains a day will be sufficient to arrest the progress of a simple intermittent within a brief time. The writer very commonly prescribes six grains, in the form of pills, three times a day; or the same amount in two doses (9 gr. each), one given in the morning at "sick-call," and one at bedtime. It is a rare thing in my experience for more than one paroxysm to occur after such treatment has been commenced.[1] Of course when patients are constantly exposed to the malarial emanations which gave rise to the attack in the first instance, the cure of an intermittent fever will not be so simple a matter, and, indeed, the arrest of the periodic paroxysmal attacks can scarcely be considered a *cure* of the intermittent fever, as relapses are very apt to occur unless further treatment is resorted to for their prevention. This failure to effect a permanent cure has been considered by some a reproach upon the fair fame of the reputed specific. Thus Pidoux says: "Are not our hospitals full of soldiers and colonists from Algeria living opprobria of cinchona? The drug has cured them twenty times."[2]

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[1] Therapeutics, Am. ed., vol. iii., p. 156.

Where the return of the disease is due to further exposure to the cause, it is certainly unreasonable to find fault with "the specific" which previously effected a cure. But those relapses which occur long after exposure and apparent cure, from the action of secondary causes, often trifling in their nature, make it necessary to admit that the cure has not been complete, and that consequently quinine is not an absolute specific.

Instead of giving quinine at stated intervals throughout the intermission, some practitioners prefer to administer it so as to secure its full physiological effects at the time of the expected return of the paroxysm. The maximum action of the drug is manifested in from two to four hours after its administration. It has therefore been recommended that the amount considered necessary be administered in two doses in such a way that the first is taken four hours and the second two hours before the expected attack (Auge).

Fayrer prefers to give quinine in solution at intervals of three or four hours during the intermission. He says:

> I have generally given it in the following form:
>
> | | |
> |---|---|
> | ℞. Quin. sulph. | gr. xl. |
> | Acid sul. dil | ʒ j. |
> | Tinct. aurantii | ʒ ij. |
> | Aqua | ℥ viij. |
>
> M. Ft. mist. One-eighth part for a dose.
>
> The diet should be light; stimulants, unless there be some special necessity, are not required. During the intervals the patient should avoid fatigue, excitement, or exposure to vicissitudes of weather; and he should continue to take quinine, after the first three or four doses, at longer intervals—say of six hours—until cinchonism begins to appear, when it may be gradually relinquished altogether. Should a second or third attack have occurred, it is well to take a dose about an hour before the onset is expected.[3]

The method of treatment recommended by Maillot and afterward by Pfeufer, in which one or two large doses—9 to 20 gr.—are to be given during the intermission, is considered by Hertz to be decidedly preferable to the administration of small doses at short intervals—*e. g.*, 2 gr. every two hours, as some authors recommend. The experience of the writer is quite in accord with this opinion; and inasmuch as the paroxysm almost invariably occurs in the daytime, the administration of a full dose at bedtime, and of a second dose at six to eight o'clock in the morning, will almost always bring the patient under the full influence of the drug in time to anticipate the daily paroxysm, if the fever be of quotidian type. In tertian intermittent, as the paroxysms commonly occur in the afternoon, the full amount may be given, in one or two doses, before eleven or twelve o'clock in the morning.

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[1] Dr. Burton Brown, of Lahore, India, says, with reference to intermittent fever in that vicinity: "The cure by large doses of quinine is so certain that we often call it four-day fever. A man gets fever one day, sends for the doctor the next, who gives him a purgative, then 15 or 20 gr. of quinine; the third day he feels weak, takes another dose of quinine with some tonic, and on the fourth day returns to his work apparently quite well" (Fayrer, op. cit., p. 108).

[2] Treatise on Therapeutics (Trousseau and Pidoux), vol. iii.

[3] Op. cit., p. 108.

Many practitioners in our own country and abroad—especially in India and in the West Indies—habitually commence the treatment of a case of intermittent fever by the administration of evacuant remedies—cathartics, emetics, or both—and this is looked upon by some as quite essential, for the reason that without this "preliminary treatment" quinine is said not to exercise its specific power. Fayrer says: "The bowels must be kept open, not merely with the object of removing accumulation, but of relieveing the portal system, liver, and spleen. Quinine will have little effect without this." There can be no doubt of the importance of this preliminary medication in certain cases, but as a method of routine practice it is to be deprecated. When the stomach is oppressed by undigested food or acrid secretions, a mild emetic is a proper remedy; when there is constipation, or diarrhœa from the presence of irritating material in the *primæ viæ*, there is no question as to the propriety of clearing out the bowels by means of a gentle cathartic, but powerful drastic purgatives commonly do more harm than good. It is true that when the gastro-intestinal mucous membrane is intensely hyperæmic or inflamed, quinine will not be readily absorbed; but in this case drastic cathartics are not likely to help the matter. A dose of castor-oil, or a seidlitz powder will often constitute the only preliminary treatment indicated; or if a mercurial cathartic is preferred, ten grains of blue mass may be given at bedtime, and a seidlitz powder or a dose of "Hunyadi Janos," the following morning before breakfast. Instead of giving the cathartic, when it is indicated, preliminary to the administration of quinine, the writer frequently commences the treatment by the administration of ten grains of blue mass and ten of quinine at bed-time. Very commonly the bowels are freely moved the following morning, and a second dose of ten grains of quinine is administered at "sick-call." Or, if required, a dose of oil or a seidlitz powder is given, and this is followed by the quinine an hour or two later.

It must be remembered that hyperæmia of the mucous membrane of the stomach and bowels, a more or less heavily coated tongue, and congestion of the liver, are among the ordinary results of malarial poisoning, and that these symptoms, as well as the febrile manifestations, will yield to specific medication. When, however, the immediate cause of the attack is some gastric or intestinal derangement, due to improper diet, overfeeding, etc., it will be necessary to direct special attention to the exciting cause, as well as to neutralize the malarial poison—or its effects. In other words, gastro-enteric complications may demand special treatment, but the cure of an intermittent fever does not require the preliminary use of evacuant remedies, as ample experience has demonstrated that it may be promptly effected by the proper administration of quinine without resorting to any preliminary treatment.

Modes of Administration.—The physiological effects of quinine may be obtained by administering it either by the mouth, by enema, endermically, or hypodermically. The sulphate, which is the salt usually prescribed, is less soluble than the muriate, but the latter is a less stable preparation. Many practitioners prefer to give the sulphate in solution, as it is thus more quickly absorbed; but well-made pills are quite as efficient, although not quite as prompt in their action. They will be preferred by most patients to the solution, which has an intense bitterness that it is hard to disguise. Some persons, however, do not object seriously to the bitter taste, and take the medicine without difficulty in solution or in powder. The powder may be enclosed in gelatine capsules or in a wafer of the same material, when there is strong objection to the bitter taste. It is said that the taste is disguised to a considerable extent by administering the medicine in syrup or fluid extract of liquorice root, in syrup of yerba santa,[1] or in milk. The favorite solvent in this country is the aromatic sulphuric acid, which should be used in the proportion of one drop to each grain of quinine in the prescription. Pills which are old and hard are not reliable, as they dissolve with difficulty, and may even pass through the whole length of the alimentary canal without being dissolved.

Dr. Sawyer, of Alabama, in an interesting paper on "The Hypodermic use of Quinine in certain Fevers," says:

> I might add, from my notes, quite a number of cases that have occurred in my practice this last fall, in addition to those already given, in which quinine administered by the stomach to persons, *of all ages*, suffering with attacks of the malarial fevers, has passed through the bowels unchanged, as well as various purgative pills, and pills and capsules of quinine twenty-four and thirty-six hours after they were taken into the stomach. This result has generally occurred without any special looseness of the bowels.[2]

An aqueous solution of quinine is promptly absorbed when introduced into the rectum by enema, and when the stomach is irritable this method of administration is preferable to that by hypodermic injection, unless a very prompt action of the drug is imperative. On account of its greater solubility the muriate is preferable to the sulphate for administration by enema.

The *hypodermic method* of administration is an invaluable resource in those cases in which the remedy is not retained by the stomach or rectum, and especially in pernicious cases in which a prompt impression is imperative. Cinchonism may be promptly induced by this mode of administration, and the quantity required is very considerably less than when the medicine is given by the mouth or rectum. According to Flint, the effect is three times greater than when given by the stomach. Notwithstanding the economy and efficiency of this mode of administration, it has not met with general favor for the cure of ordinary intermittent and remittent fever, although strongly recommended by some physicians to the exclusion of all others. This is largely due to the fact that, in the hands of many practitioners, more or less inflammation, and the formation of painful abscesses at the point of insertion, has been a not infrequent result of these hypodermic injections; and to the reluctance of most patients to submit to the slight pain attending the operation, which is not so trifling from their point of view as from that of the surgeon. For these reasons it is doubtful whether the economic advantages of this method will suffice to bring it into general use, although it has already been quite largely employed in hospital practice, and the danger of the formation of abscesses, when a proper solution is employed, has probably been much exaggerated.

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[1] J. K. Lilly, in Chicago Med. Rev., August 15, 1882.

[2] Virginia Medical Monthly, January, 1882, p. 730.

Dr. Moore,[1] of the Bombay Medical Service, believes that the production of inflammation is due to quinine in suspension, and when a good solution is used he has never seen the slightest inflammation or irritation follow the operation. He uses a solution containing thirty grains of quinine to half an ounce of water, dissolved by means of eight or ten drops of dilute sulphuric acid. Of this from half a drachm to a drachm is injected. This author reports that the pain is trifling, "not greater than the prick of a pin," and that his patients prefer to submit to the operation rather than "taste the bitter of quinine." The method was employed "in upward of thirty cases of intermittent fever, and in several cases of remittent, and with almost invariable success, the former class seldom requiring a second application, the latter generally recovering after the fifth or sixth injection.

Mr. A. S. G. Jayakar[2] has also extensively employed this method in hospital practice, in India, and reports that:

> In most cases the first dose was quite sufficient to put a stop to any further attack of fever. . . . But above all, the most marked beneficial effects of the hypodermic injection of quinia may be observed in cases of brow ague, or hemicrania, dependent for its cause on malaria. . . . The suffering of the patient, which is sometimes excessive and most unbearable, sufficient to make one mad, calls at our hands for an immediate means of relief, and such a means we have in the hypodermic injection of quinia. To the patient's great surprise and joy he finds himself, within five to ten or fifteen minutes, either greatly relieved or entirely cured.

Dr. Patterson, Surgeon-Superintendent of the British Seaman's Hospital at Constantinople, reports that the treatment of the various forms of intermittent fever by hypodermic injection has been practised in that hospital since 1869 (report made in 1876).

> Two-grain injections were first tried: a short experience proved one grain to be sufficient. In pronounced quotidian and tertian, without complication, where the interval between the paroxysms is clearly defined, the treatment is of the simplest character. Two hours or less before the anticipated paroxysm the patient is sent to bed, and one grain of sulphate of quinine, dissolved in eight minims of warm water, with the least possible quantity of diluted sulphuric acid, is injected deeply into the subcutaneous cellular tissue of the upper arm, over the deltoid, or in the gluteal region. He is then covered up and a basin of warm tea given. This small dose sometimes prevents the return of the paroxysm: it always modifies it. This is repeated three or four times in succession, and the patient is cured. No other medicine is given in the interval, except a laxative if required. One hundred and eighty-five such cases were under observation from ten to twenty days after discharge from hospital. Relapse was rare, and was almost always traceable to drink. . . . The danger of suppuration arising at the point of insertion has been objected to; but this may be avoided if the needle be carried deep into the cellular tissue. I have only seen it happen three times, and in all three cases the patients were convalescents from Brindisi fever, and in a state of extreme debility. These remarks are based on the careful observance of more than two hundred cases treated by my colleague, Dr. Zelrowsky, and myself. We believe the muriate of quinine to be less active than the sulphate when thus administered.[3]

Dr. Lente, of Duchess County, N. Y., has employed this method very extensively and reports as follows:

> To recapitulate: This method would seem, in the light of our present experience, to be particularly applicable to those fatal cases of the disease called "pernicious" or

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[1] W. G. Moore, L.R.C.P. Ed. London Lancet, 1863, p. 660.

[2] Indian Medical Gazette, July 1, 1871.

[3] Medical Times and Gazette. London, July 15, 1876.

"congestive fever," in which no reaction—or a very imperfect one—takes place, and a patient dies, as in the collapse of cholera, because neither the stomach nor rectum will absorb medicine, even if they could retain it and there were time for it to act; to cases where vomiting is persistent, or where intense pain or other distress is a prominent symptom; to quotidians, where the paroxysm is so protracted as to afford little time for the action of remedies by mouth or rectum; to patients who cannot tolerat equinine on account of cerebral symptoms; and to the cases of the poor and of laboring men, where promptness in action and cheapness of material are important considerations. Indeed, in an economic view, especially in the case of armies, hospitals, and eleemosynary institutions, its advantages are very manifest, particularly in regions where the doses by the mouth need to be enormous; and from all parts of the world, temperate as well as tropical, where malaria prevails at all, we have reports of the necessity of these extreme doses in certain cases of epidemics.

The production of inflammation, abscess, or sloughing is believed to be due to the irritant character of the injection employed; and after having tried various solutions, Dr. Lente finally adopted the following as the most suitable: Quinine, 50 grains; dilute sulphuric acid, 100 minims; carbolic acid, 5 minims, and water, one ounce. The quinine and water are heated to a boiling point in a porcelain dish placed over a spirit-lamp, the sulphuric acid being added while stirring with a wooden spatula. The solution is at once filtered into a bottle and the carbolic acid added. This solution causes as little irritation as injection of morphia, or other substances of smaller bulk, for all hypodermic injections, however small, will occasionally induce inflammation, abscess, or even sloughing.[1]

Dr. N. L. Guice, of Georgia, has used an acid solution, hypodermically, for sixteen years, and has never seen any worse result than the formation of a cold abscess containing a few minims of pus. He attributes his success to the care taken in making the injection. This consists in avoiding laceration or even *tension* of the tissues.

The hypodermic injection of the sulphate of quinine, dissolved by means of dilute sulphuric acid, having, in the hands of some practitioners, given rise very frequently to inflammation and abscess, other solutions have been proposed as a substitute for this, and some of them doubtless possess advantages over it. The bisulphate, which is quite soluble, is one of the best, and is extensively used in the treatment of pernicious fevers in the vicinity of Rome. Dr. G. Pettacci of that city recommends the following: Quinine bisulphate 2 grm., dissolved in 20 grm. of distilled water. The whole of this amount is sometimes injected beneath the integument in the epigastric region, and yet Dr. Petacci says that these injections are not followed by the formation of abscess or other serious consequences if a proper solution of the bisulphate is used.

> In order to avoid so many perforations of the skin, each time I introduce the canula I inject through it successively three syringefuls, injecting slowly, not to produce too much irritation and to render absorption more easy.[2]

The bisulphate is still more soluble in glycerine, dissolving with heat, in the proportion of one part in three. This solution is said to keep well and permits of the introduction of 10 to 15 gr. with each syringeful (Whittaker).

The hydrochlorate is also more soluble than the sulphate and contains a larger proportion of quinia. This salt is recommended by Köbner,[3] who gives the following formula for a solution for hypodermic use: Quinine hydrochlorate, 0.5 to 1.0 grm.; glycerin., aqua destill., āā, 2.0 grm. This amount would answer for four injections.

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[1] Paper read at the Dutchess County Medical Society. New York Medical Journal, March, 1874.

[2] N. Orl. M. & S. J., June, 1880, p. 1128.

[3] A. J. M. Sc., Jan., 1881, p. 281 (from Der Practische Artz, March, 1880).

Another salt of quinia which possesses special advantages and is probably the best adapted for hypodermic use is the bromohydrate. This has been used quite extensively of late, and is especially recommended by Gubler, Soulez, Whittaker, and others. This salt dissolves in fifteen parts of water (with heat), or in four parts of glycerine. Whittaker says with reference to its use:

> Soulez recommends the use of alcohol and Rosenthal of glycerine in its preparation, and perfect solutions may be readily made in either way, so that an ordinary syringeful will introduce fifteen grains of the salt But there are objections to both methods of preparation Alcohol irritates the tissues and glycerine makes a thick solution, almost too thick for ready passage through a fine needle, and probably too thick for ready absorption. I have in practice entirely discarded all vehicles except water, and rely solely upon heat to obtain a perfect solution. I have a druggist put into a test-tube twenty grains of the bromide of quinine and add to it two drachms of water. The tube should be corked, not to preserve the substance, for it is still crystalline in this proportion, but for cleanliness. To use the drug, all that is necessary is to heat the tube over a gas flame, coal-oil lamp, or other means of illumination. The tube should be held above the light, of course, and not in it, that it be not smoked, and hence rendered opaque. Two or three minutes suffice to reduce the quinine to a limpid crystalline fluid in the tube. Then it is poured in sufficient quantity into a teaspoon, previously warmed by holding one minute over the flame, and from the spoon it is taken up into the syringe, warmed also in the same way, and is ready for use, which must be immediate. It may be injected anywhere, but always *under* and never *into* the skin. The ordinary syringe contains half a drachm, and this introduces about five grains at a time.[1]

A solution of the sulphate of quinine made with tartaric acid and distilled water has been recommended by several authors—Bourden,[2] Schriven,[3] Dixon,[4] Sawyer,[5] and others. This is said to be far less likely to induce inflammation than the solutions made with a mineral acid. One part of quinine, one-half part of tartaric acid, and twenty parts of distilled or boiled (Sawyer) water is said to make a good solution.

The following has also been recommended as "a perfect solution for subcutaneous injection:"[6]

℞. Quin. sulph.	100 grs.
Ac. hydrobromic.	ʒ j.
Spts. frumenti ad	℥ j.

M. Dissolve and filter.

There is considerable difference of opinion as to the value of the *endermic* method of administration, and without doubt it is inferior to all others, and only to be recommended in the case of children, when it is impracticable to give the medicine by the mouth or by enema. Some practitioners in the South are in the habit of treating intermittent fever in young children by this method, and resort to frictions made with the sulphate or muriate of quinine rubbed up with lard. The writer has been assured that this treatment is quite successful, and has himself adopted it in two or three instances with good results. The oleate, made by dissolving the alkaloid in oleic acid, is no doubt a preferable preparation for external application. The fact that it may be absorbed in sufficient quantity to produce the physiological effects of the drug seems established by the following observations, recorded in an editorial article in the *North Carolina Medical Journal:*

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[1] Professor James G. Whittaker, in the Cincinnati Lancet and Clinic, Oct. 9, 1880.

[2] Med. Times & Gaz., Lond., March 8, 1873.

[3] Lancet, Lond., 1876.

[4] Southern Med. Record, May 20, 1882.

[5] Va. Med. Month., Jan., 1882.

[6] Pacific Med. Jour.

> We have had some recent experience, which, although confined to one case, tests the matter very thoroughly. A patient having a great antipathy to quinine was seized with a fever of a malarial type and of great irregularity as to its course. It was determined to attack it by the use of oleate of quinine epidermically, both for the reason of the antipathy the patient had for the remedy by the mouth and because the exacerbation was irregular, and a continuous impression of the remedy was necessary. The oleate was prepared of the strength, at first, of one drachm of quinine (alkaloid) to two ounces of the acid, which was increased in strength to double the quantity of the alkaloid. The inunctions were made at intervals of eight hours, consuming the two-ounce mixture during that time. The patient recognized cinchonism distinctly, but as the temperature occasionally reached 102.5° in the afternoon the stronger oleate was applied. From this time daily tests were made of the urine, and despite the abundant coloring matter contained in it, quinine was distinctly visible by its green reaction with chlorine. Tests of the urine were continued several days after the cessation of the inunction and quinine was detected. The inunctions in this case were made over a large area of surface, but particularly in the groin and the inner side of the thighs and abdomen, and covered with water-proof paper to prevent absorption by the sheet. The friction was continued for a sufficient length of time to excite the skin to absorption, leaving very little unabsorbed oleate on the surface.

It must be remembered in administering quinine that this invaluable remedy may do harm as well as good, and that in excessive doses it has pronounced toxic effects. Some persons also, from idiosyncrasy, are unpleasantly affected by moderate or small doses. Dr. Bryce, of Richmond, Va., relates a case in which fifteen grains at a single dose produced most alarming symptoms of collapse in a lady patient. He says:

> I have time out of mind seen cases of intermittent fever in which the chill had been anticipated and warded off by the timely use of the remedy, but in which the patients for hours would be terribly depressed. They would have the soft, clammy skin, the weak, compressible pulse, the sighing and labored respiration, all of which indicates nervous shock and threatening collapse, and this is all due to the profound impression of quinine upon the nervous centres.[1]

Dr. Henry F. Campbell,[2] of Augusta, Ga., has also witnessed the most alarming heart-perturbations and "sinking" as an occasional result of the administration of quinine.

These exceptional results from moderate doses, and the cases on record in which fatal poisoning has occurred from larger doses, call for caution in the administration of this remedy, which is sometimes given in the most reckless manner. It is doubtful whether a dose exceeding forty grains is ever required in the most threatening cases of malarial toxæmia, although much larger doses have been given by Maillot and others without apparent injury to the patient. We have already remarked that persons under the influence of the malarial poison have an exceptional tolerance for quinine. Quinine in excessive doses may also give rise to partial deafness and to amaurosis of a more or less permanent character. On the other hand, neuralgic pains, debility, dropsy, and a variety of symptoms due to chronic malarial poisoning are often ascribed by ignorant persons to the use of this remedy, and the medicine which has time and again arrested the progress of an intermittent fever, and perhaps saved the life of the individual, is held responsible for every ache and pain he may suffer for years afterward.

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[1] C. A. Bryce, M.D., in the Medical Herald, Louisville, Ky., Feb., 1883.

[2] The Prophylactic and Therapeutic Value of Quinine in Gynecic and Obstetric Practice, Tr. Am. Gynec. Soc., vol. v. (1881).

The most common and distressing immediate effect of quinine due to idiosyncrasy is the occurrence of a cutaneous eruption, which may be simply an efflorescence or may present the features of urticaria. It is attended with tumefaction and intense itching, and in some cases the mucous membrane of the oral and nasal cavities is also involved, and is intensely hyperæmic. The conjunctivæ also are injected, and there is lachrymation, sneezing, and sometimes distressing dyspnœa. Bromide of potassium is said to moderate the severity of these symptoms, and morphia very soon relieves them (Campbell).

According to Professor Gubler,[1] whose conclusions have been confirmed by Soulez,[2] the bromohydrate of quinine is less liable to produce quinine intoxication and the unpleasant symptoms sometimes resulting from the use of the sulphate, and yet equals or excels the last-named salt in therapeutic value. It should, therefore, be given the preference in those cases in which experience has shown that the sulphate is not well tolerated. When this salt is not at hand hydrobromic acid may be given in combination with the sulphate of quinine for the relief of headache, *tinnitus aurium*, and other nervous troubles in those who are especially subject to these symptoms. Or the hydrobromate may be prepared in accordance with the following formula, which is given in the National Dispensatory :

℞.	Potassii bromid	162 gr.
	Acid tartaric	198 gr.
	Quiniæ sulph	60 gr.
	Aquæ	f℥iij.

M. Filter. Dose, thirty minims to one fluidrachm.

Dr. Eagan,[3] of Texas, says that when quinine is not tolerated, owing to idiosyncrasy, it may be given without bad effect in combination with diluted hydrocyanic acid, ten drops being given as a medium dose. It is also asserted that quinine intoxication may be relieved by ergot.[4]

Much difference of opinion has existed among physicians as to the alleged oxytocic power of quinine. According to some this drug may induce premature contractions of the uterus, and abortion, in pregnant women ; others deny this, but accord to it the power of increasing the force of uterine contractions when labor has commenced ; and others deny that it has any oxytocic power whatever. We are here only concerned with the use of the drug in the cure of malarial fevers, and have no hesitation in saying that it should be promptly administered to pregnant women suffering from any form of malarial disease, as the most efficient and speedy means of effecting a cure. This is especially imperative in these cases for the reason that the paroxysmal febrile attacks induced by malaria often cause abortion, while the power of quinine to do so is extremely problematic. There can be little doubt that abortion due to malarial poisoning has been not infrequently ascribed to the administration of quinine, which perhaps, if given more promptly or in more efficient doses, might have prevented the accident.

This fact is generally recognized by practitioners in the decidedly malarious regions of the United States, and it is only in those localities where malarial fevers are rare that physicians are likely to hesitate in resorting to the use of this specific, because their patients are pregnant. We believe that the following quotation from a recent paper by Dr. Henry F. Campbell, of Augusta, Ga., is in accordance with the experience of practitioners throughout the most malarious sections of the South:

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[1] Journal de Thérapeutique, July 10 and Sept. 10, 1875.

[2] Gaz. Hebdom., Feb. 18, 1876.

[3] N. Orl. M. & S. J., Oct., 1868, p. 703.

[4] Med. Times, Phila., p. 846. Aug. 25, 1883.

> At a period not very remote from the present, though I have not seen much concerning it of late, the medical journals of this country contained frequent articles discussing, and most of them strongly asserting, the oxytocic properties of quinine. The tendency and the precept of all these papers was to lead to the establishment of the opinion that the preparations of cinchona are not only inapplicable, but positively dangerous and subversive, in any and all the stages of pregnancy. Abortions, miscarriages, and premature labors were constantly attributed to its administration. Why this fusilade against this prominent and important article of the pharmacopœia should have ceased, I am at a loss to divine, unless upon one or other of two very different assumptions; either "the sword was sheathed for lack of argument," as no one seemed to challenge the statements, or it was considered that the fact was too thoroughly established to require either reassertion or farther confirmation.
>
> To this opinion in regard to the action of quinine under a proper, or in any degree prudent, application of the agent, my own daily observation for nearly forty years gives an unconditional denial. "Woe to her that is with child!" would it indeed be, to all the women of our malarial districts of the South, and in many portions of the West, did quinine, the daily and long-continued taking of which constitutes an important condition of their very existence, produce such calamitous results! The very suggestion of the circumstances, without argument, must certainly at once refute all charges against quinine as an oxytocic. We have only to be reminded of the thousands of pregnant women who must daily use the drug to prevent or to break the force of paroxysms of fever, and to know the fact that the question of such an effect never enters the mind of either patient or physician on its administration, to be fully convinced of the fallacy regarding its abortivant effects. Notwithstanding all that has been written on the subject, and though many of them are fully aware of the charges of oxytocic properties made upon quinine, I do not know a single practitioner in the widely extended region of the South with which I am familiar, who is at all influenced by them or who would hesitate to administer quinine freely to a pregnant woman at any stage, as the very *sheet-anchor* of her safety in paroxysmal fever.[1]

Next to quinia and its salts we must place the *other cinchona alkaloids*, as antiperiodic remedies. The physiological effects of these alkaloids are not, however, identical with those of quinine, and M. Laborde[2] claims that the effects of quinia and cinchonia are of an opposite nature, one producing stupor and the other (cinchonia) violent epileptiform convulsions, when administered hypodermically to the lower animals.

Bochfontaine,[3] also, states that cinchonine produces more decided convulsive effects and that quinine is the more powerful toxic agent. Nevertheless, he finds that the physiological effects of these alkaloids and of cinchonidine are similar, and that they all depress the central nervous system after momentarily exciting the circulation.

We have a recently reported case of poisoning by sulphate of cinchonidine in which convulsions occurred at first, followed by symptoms of collapse similar to those induced by a toxic dose of quinine. The temperature fell to 94.6°, the pulsations at the wrist became imperceptible, the pupils dilated, the skin and mucous surfaces entirely bloodless, and the patient—a boy five years old—died "apparently from exhaustion." The amount taken was one hundred and twenty-eight grains, which, by a mistake in the dose, was administered within six hours.[4]

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[1] Op. cit. (p. 2 of reprint of paper referred to).

[2] Le Progrès Médical, No. 45.

[3] Revue Scientifique, Feb. 24, 1883.

[4] Case reported by Dr. Jos. E. Winters. The Medical Record, Feb. 2, 1884.

The results of the experiments made in India by a Medical Commission appointed by the Indian Government to ascertain the comparative therapeutic value of the cinchona alkaloids are summed up as follows :

> In regard to the relative effects of the three new alkaloids, and with them chemically pure sulphate of quinia, the evidence derived from their use shows that, with the exception of sulphate of cinchona, as already stated, they in a remarkable degree so closely resemble each other in therapeutical and physiological action as to render distinctive description of little or no practical utility.
>
> In reviewing the whole of the operations for testing the therapeutical effects of the chinchona alkaloids, the result confirms generally the favorable opinion expressed by the Commission last year, and likewise conclusively establishes beyond doubt that ordinary sulphate of quinia and sulphate of quinidia possess equal febrifuge power ; that sulphate of chinchonidia is only slightly less efficacious ; and that sulphate of cinchonia, though considerably inferior to the other alkaloids, is, notwithstanding, a valuable remedial agent in fever.[1]

Dr. Joseph Ewart had previously experimented with these alkaloids, and arrived at results in conformity with this report. He says of the sulphate of cinchonia, that while undoubtedly possessed of antiperiodic power, in doses of 10 to 20 grains, it is objectionable because of the irritability of the stomach induced by its administration.[2]

A more recent report by Dr. Joseph Dougall, of the Madras medical service, is to the following effect :

> In the trials made with the three alkaloids, they were used in succession indiscriminately as suitable cases occurred. Quinidia was given in 39 cases, cinchonidia in 35, and cinchonia in 34. The 16 cases of tertian were equally distributed among the three remedies. The whole 108 cases recovered, but in one the disease passed into remittent fever unchecked. In 27 cases there was either no paroxysm at all after the first doses, or a very mild one merely, although the alkaloid was given during a single day only. In 30 others the treatment required to be continued only two days, and in 14 others for three days. Thus, in 71 cases, or almost two-thirds, the fever was arrested within that period. In 3 only was it necessary to prolong the treatment to ten, twelve, and thirteen days.
>
> There was very little difference between the alkaloids in the necessary duration of treatment. But a difference was observed in the doses required. The average doses of quinidia varied between 31 and 70 grains, of cinchonia from 54 to 76, of cinchonidia from 43 to 90. Extreme cases are excluded from this calculation, because tending to vitiate the result. The conclusion is that quinidia is the most powerful, cinchonidia next to it, and cinchonia the least active ; but that even cinchonia is energetic, and in an adequate dose a sure remedy.
>
> Quinidia appearing to be the most energetic of the alkaloids after quinia, some experiments were made on its physiological effects in the healthy state of the body. From trials on my own person, a dose of 10 to 15 grains, taken three hours after a light breakfast, occasioned severe nausea, afterward slight griping, and in three hours one or two rather loose bilious discharges from the bowels Twenty grains occasioned in twenty-five minutes so much nausea that vomiting could be restrained only by assuming the horizontal posture for an hour. In three hours three or four copious liquid bilious evacuations ensued. Twenty-five grains always induced vomiting, no matter what precautions were observed. These results will explain in some measure the physiological phenomena which often attended its curative action.[3]

A report by Surgeon-Major George Hunter, made in 1875, with reference to the value of sulphate of cinchonidia, is not so favorable. He arrives at the conclusion that this alkaloid is greatly inferior in value to quinia, and has no advantage over it in an economic point of view.[4]

The mixed alkaloids of the bark of *cinchona succirubra*, a tree which grows in abundance in East India, Ceylon, and Java, are decidedly cheaper than the salts of quinia, and have been used successfully by Vinkhuysen, Chevers, Ewart, Hollis, and others. The name *quinetum* has been given by Dr. De Vry to these mixed alkaloids, and the sulphate has been found by an English chemist [1] to contain twenty-five to thirty per cent. of quinine sulphate ; fifty to fifty-five per cent. of cinchonidine sulphate ; and twenty to twenty-five per cent. of cinchonine sulphate.

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[1] Lancet, Lond., May 21, 1870.

[2] Indian Annals of Medical Science, Jan. 1869.

[3] Edinburgh Med. Journ., Sept., 1873.

[4] Lancet, Lond., May 15, 1875.

Dr. Vinkhuysen, physician to the household of H. M. the King of the Netherlands, has prescribed quinetum extensively and arrives at the following conclusions :

1. The only malarious disease in which quinetum cannot be employed in place of quinine is pernicious fever. Quinetum requires more time to act than quinine, and as rapidity of action is absolutely necessary in this disease, quinetum cannot be used in it as a substitute for quinine.
2. In all forms of pure malarial intermittent fever, quinetum has the same apyretic effect as quinine, but is less powerful and acts more slowly. It must therefore be given in large doses and at longer intervals before the ague fit, than quinine.
3. Quinetum does not produce the unpleasant and even dangerous symptoms of quinine when given during the fit, and may be taken during the fit without causing any unpleasant feeling.
4. Quinetum never causes noises in the ear.
5. Persons who are liable to suffer from the toxic effects of quinine, and who therefore cannot take it without the greatest discomfort, can take quinetum without this unpleasant effect, and yet obtain a similar therapeutical result.
6. The influence of quinetum in chronic cases is greater than that of quinine.
7. The tonic action of quinetum is similar, and perhaps even greater, than that of quinine.
8. The action of quinetum in cases of masked or larval malaria, and especially in rheumatic affections due to malarious influences, is incomparably greater than that of quinine.[2]

An antiperiodic remedy which has been extensively used in India, and is strongly endorsed by Professor Maclean, is known as "Warburg's Tincture." The composition of this was for a long time kept a secret, but the formula has now been published, and there can be no doubt of its value, inasmuch as the *disulphate of quinine* is the principal ingredient.

The following is the formula for its preparation :

℞. Aloes (socotr.) libram ; rad. rhei (East India); sem. angelicæ ; confect. fect. damocratis ; [3] ana uncias quatuor.

Rad. helenii (s. enulæ) ; croci sativi ; sem. fœnicul. ; cret. præparat. ; [4] ana uncias duas.

Rad. gentianæ ; rad. zedoariæ ; pip. cubeb. ; myrrh. elect. ; camphor ; bolet. laricis : [5] ana unciam.

The above ingredients are to be digested with 500 oz. proof spirits in a water-bath for twelve hours ; then expressed, and 10 oz. of disulphate of quinine added ; the mixture to be replaced in the water-bath till all quinine be dissolved. The liquor, when cool, is to be filtered, and is then fit for use.

The mode of administering it is as follows :

One-half ounce (half a bottle) is given alone, without dilution, after the bowels have been evacuated by any convenient purgative, all drink being withheld. In three hours the other half of the bottle is administered in the same way. Soon afterward, particularly in hot climates, profuse, but seldom exhausting perspiration is produced. This has a strong aromatic odor, which I have often detected about the patient and his room on the following day. With this there is a rapid decline of temperature, immediate abatement of frontal headache—in a word, complete defervescence—and it seldom happens that a second bottle is required; if so, the dose must be repeated as above. In very adynamic cases, if the sweating threatens to prove exhausting, nourishment in the shape of beef-tea, with the addition of Liebig's extract, and some wine or brandy of good quality, may be required.

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[1] Mr. Whiffin, of Battersea (quoted from a paper by Dr. W. Ainslie Hollis, in the British Medical Journal, May 10, 1879).

[2] The Practitioner, Lond., Feb., 1878, p. 81.

[3] This confection, which consists of an immense variety of aromatic substances, was once officinal, and is to be found in the London Pharmacopœia, 1746.

[4] Dr. Warburg informs me that this ingredient was added to correct the otherwise extremely acid taste of the tincture. Many other substances were tried, but none answered so well as prepared chalk.

[5] This is the Polyporus Laricis (P. officinalis, Boletus purgans or Larch Agaric), "formerly," says Pereira, "used as a drastic purgative, and still kept by the herbalist."

"It will be seen," says Professor Maclean, "that quinine is the most important ingredient in the formula, each ounce bottle containing nine grains and a half of the alkaloid. Its presence has been detected by every chemist who has attempted its analysis, and never doubted by any medical man of experience who has used the tincture. Many will say 'after all, this vaunted remedy is only quinine concealed in a farrago of inert substances for purposes of mystification.' To this objection my answer is: I have treated remittent fevers of every degree of severity, contracted in the jungles of the Deccan and Mysore, at the base of mountain ranges in India, on the Coromandel coast, in the pestilential highlands of the Northern Division of the Madras Presidency, on the malarial rivers of China, and in men brought to Netley Hospital from the swamps of the Gold Coast, and I affirm that I have never seen quinine, when given alone, act in the manner characteristic of this tincture. And, although I yield to no one in my high opinion of the inestimable value of quinine, I have never seen a single dose of it given alone, to the extent of nine grains and a half, suffice to arrest an exacerbation of remittent fever, much less prevent its recurrence; while nothing is more common than to see the same quantity of the alkaloid in Warburg's Tincture bring about both results."[1]

Next to the cinchona alkaloids we must place *arsenic* as a remedy for the periodic fevers. It cannot be relied upon in pernicious intermittent, but we have ample testimony as to its therapeutic value in simple intermittent, although it is less useful in quotidian ague than in the tertian and quartan types. It is especially suited to the treatment of chronic malarial cachexia, and of relapses due to secondary causes, and occurring some time after exposure to malarial influences. In these cases it often effects a cure after quinine has failed.

Morehead considers half a grain of arsenious acid about equivalent in power to fifteen grains of quinine. According to this author one-eighth to one-fourth of a grain—equal to fifteen to thirty minims of Fowler's solution—given in the intermission, "has no evident antiperiodic power." But twice this amount is sufficient to prevent recurrence in mild intermittents in India.

It may be exhibited with safety in this quantity in cases in which there is no tendency to gastric or intestinal irritation, and most advantageously in repeated doses of ten minims or less, sometimes combined with a few minims of tincture of opium."[2]

These doses will seem "heroic" to most American practitioners, but M. Boudin does not hesitate to give still larger doses. His method of using the remedy, as communicated to Morehead, is as follows:

Arsenious acid, 1 grm.; distilled water, 1,000 grm.; boil for fifteen minutes. Add white wine, 1,000 grm.

One hundred grammes of this liquid represent five centigrammes, or one grain, of arsenious acid. We give in Paris, on the average, a half-grain per day during the interval between the paroxysms. But one may give more. *It is important to divide the dose as much as possible.* The tolerance for arsenic is less as the fever disappears. The first sign of intolerance is salivation (l'eau à la bouche). We must profit by the patient's tolerance in order to saturate him. It is necessary to continue the remedy for a longer

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[1] Medical Times & Gaz., Lond., Nov. 13, 1875.

[2] Morehead, op. cit., p. 33.

> or shorter period after the cessation of the fever. The end I have in view is to oppose to the malarial diathesis an arsenical diathesis.[1]

That arsenic may be given in these heroic doses without injury to the patient is possible, but it certainly would not be wise to administer it in such quantities without observing the rules laid down by M. Boudin, and especially without keeping the patient under close observation.

M. Sistach, who has used this remedy very extensively in Algeria, and with favorable results, does not find it necessary to resort to such large doses. He says: "We must begin by giving from 3 to 5 ctgr. daily (.45 to .75 gr.). After the paroxysms have ceased to recur, the dose ought to be diminished by one centigramme every day; but the patient must continue to take about one centigramme each day for about ten days after he is apparently free from symptoms." The rules of administration, laid down by this author are the same as those given by Boudin, viz: The arsenious acid must be given in solution; *it must be freely diluted, and given in very small doses frequently repeated;* and the quantity given during the twenty-four hours must bear a relation to the severity of the fever.

M. Sistach treated with arsenic 229 cases of intermittent fever in the military hospital of Bona, in Algeria; of these 136 were quotidian, 74 tertian, 11 quartan, 5 irregular, and 3 masked. The average number of paroxysms after the commencement of treatment was, for the quotidian type 1.7; for the tertian type it was but .75. This is certainly a very favorable result, and gives support to the statement of the author who reports it, to the effect that the failures which have been reported by other observers must be attributed to their neglect of those details upon which the certainty and safety of arsenical medication depends.

Colin says:

> Notwithstanding the good results obtained by these clinicians[2] and by the greater number of those who have adopted their method, we confess that we have not ventured to put it in practice in order to combat the fevers of Rome and of Algeria; we have feared at first the uncertainty of the method, which is recognized and proclaimed by that one, even, who has been its most ardent promoter: "A very remarkable fact is that the degree of efficacy of the arsenical preparations in the treatment of intermittent fevers may be influenced in a very evident manner by the reigning medical constitution, in such a way that we may see them lose in a great degree their febrifuge power, when a few days before no intermittent fever resisted their heroic administration" (Boudin).[3]

Notwithstanding this hesitation to use arsenic in the manner prescribed by Boudin and his followers, Colin admits that the danger of arsenical poisoning from such quantities administered in fractional doses, as directed, has been overestimated.

It is doubtful whether the solution employed by Boudin has any advantages over Fowler's solution—liquor potassæ arsenitis—which is the preparation commonly employed by English and American physicians. But it may be that we would be more successful in the use of this remedy if it were given in larger doses at the outset, for a day or two, for the purpose of promptly arresting the disease, rather than in moderate doses continued for some days. We have the testimony of the experienced English clinician, Morehead, that this may be done with safety, and it is undoubtedly true that gastric irritation may be avoided by giving the remedy greatly diluted and in small and repeated doses, and that this method of administration is preferable to the routine practice of prescribing five to ten drops of Fowler's solution three times daily. Wood fixes the dose at ten drops three times a day and says:

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[1] Op. cit., p. 33.

[2] Boudin, Maillot, Fremy, Sistach.

[3] Op. cit., p. 393.

> It may be continued until the disease is arrested, or until some œdema of the face, oppression of stomach, general tremors, or feelings of muscular weakness evince the action of the medicine. It must then be suspended lest the poisonous effects of arsenic should be produced. I have known a case of universal anasarca apparently arise from its use in a child. It cannot, in general, be continued with propriety much beyond a week. For infants the dose must be diminished in proportion to the age. To a child a year or two old, a drop or two may be given three times a day.[1]

Hertz says: "A cure is sometimes accomplished in a few days; oftener, however, after it has been used for two or three weeks."[2] This author considers Fowler's solution the most useful preparation, and recommends its administration in doses of eight to thirteen drops, given twice or three times a day. If the cure, with these doses, requires from a few days to two or three weeks, it may be questioned whether the continued use of the remedy during this period is not more injurious than the larger and efficient doses recommended by Boudin, which only require to be continued for a day or two. It would seem that, if for any reason, such as economy, idiosyncrasy of patient, or objection to the bitter taste of quinine, we are compelled to resort to the use of arsenic for the cure of intermittent fevers, we will do well to be guided by the experience of the French physicians with reference to its administration.

A medicine which has of late been much praised as an antiperiodic, and which is placed by Hertz next to the cinchona alkaloids, is obtained from the leaves of the *Eucalyptus globulus*, an Australian tree which has been extensively introduced in the malarious regions bordering upon the Mediterranean, and elsewhere, because of its reputed power to neutralize malarial emanations from the soil.

Eucalyptol has been found by experiment to resemble quinine in its physiological action upon the lower animals, and there is considerable clinical evidence in favor of its therapeutic value in malarial diseases.

The reports, however, are to some extent contradictory, and taking the most favorable view of them, it must be admitted that the remedy is not likely to take the place of quinine. Hertz thinks the remedy more applicable to old and protracted cases than to recent ones. Dr. Joseph Keller, chief physician of the Austrian Railway Company, has treated (1872) 432 patients with the tincture of eucalyptus, and reports that of these 310 (71.76 per cent.) were perfectly cured, and 122 (28.24 per cent.) required to be afterward treated with quinia. In 202 cases no paroxysm occurred after the first dose; in 108 cases one or more paroxysms occurred after treatment was commenced. This is the most favorable report we have seen, and we are inclined to think that a more just estimate of the value of eucalyptol will be gained by a perusal of the following summary statement by Burdel, of the results of his extended trials with the remedy.

This author says:

> The action of this remedy, which may certainly be considered a febrifuge, is slow and far from being always constant. In mild intermittent fever, eucalyptus is successful in four-fifths of the cases; in tertian, in three-fifths only; and, finally, in quartan fevers, it almost entirely fails: that is to say, in eight-tenths of the cases. In the

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[1] Practice of Medicine, vol. i., p. 273.

[2] Ziemssen, vol. ii., p. 672.

seasons when intermittent fever is most frequent—that is to say, endemic—relapses are much more common when eucalyptus is used than when recourse is had to quinia. Relapses may, however, be avoided by administering eucalyptus more frequently after some days' rest only, and in as large doses as the stomach will tolerate. This remedy is perfectly inert in palustral cachexia. Finally, M. Burdel believes that in the second year of his experiments he obtained a rather larger proportion of cures and a smaller number of relapses, because he gave the eucalyptus in conjunction with good wines, iron, and quinia, and kept the organism up to its work by frequently repeated doses. Dr. Burdel administered the alcoholic extract of eucalyptus in pills, each containing fifteen centigrammes, to the number of from four to ten daily, according to the form of the fever, given twice during the day.[1]

Some very favorable reports have been made as to the value of *iodine* as an antiperiodic remedy; but as most of these are from physicians engaged in dispensary practice, who have not been able to obtain a complete history of a majority of the cases treated, it is necessary to receive them with some caution. We would remark, also, that city malaria is not always the same thing as country malaria, and that when we read that almost uniform success has been attained in the treatment of over 300 cases of malarial affections at the St. Louis Free Dispensary,[2] our faith in the remedy as a cure for ague is somewhat shaken by learning that under the heading malarial affections are included "neuralgia, headache, diarrhœa, dysentery, etc."

Morison,[3] who reports 250 cases treated in dispensary practice in Baltimore, is very favorably impressed as to the value of the remedy and says:

> The dose given has been invariably, for an adult, 15 minims—not drops—three times a day, a quarter of an hour before meals, largely diluted. . . The record of the 250 cases is as follows: Number of cases not heard from after the first visit, 150. Number of cases heard from a second, third, or more times, 100. Of the cases heard from, 84 are on record as cured, 2 not cured, and 14 in which neither iodine or cinchonidia effected a cure.

The evidence given by Dr. Grinnell[4] is still more definite. Being situated in an intensely malarious region—Witchita Agency, Indian Territory—and having exhausted his stock of quinine, Dr. Grinnell decided to resort to the use of iodine, as recommended by the Russian physician Nonadnitzchauski. The dose given was ten to twelve drops of the tincture in half a glassful of sweetened water, every eight hours. The results far exceeded his most sanguine expectations, and he arrived at the conclusion that the antiperiodic power of iodine is superior to that of any other remedy known, with the exception of quinia; 135 cases of intermittent fever, principally of the quotidian and tertian types, were treated in this way, with results fully equal to those to be obtained by the use of the sulphate of quinine. The remedy seemed to have a magical effect, and in many cases there was no recurrence of the paroxysms after the commencement of treatment; the medicine was however continued for two or three days after the cessation of the fever. In cases of enlarged spleen the size of the organ was more speedily reduced than when quinine was used. Willibrand,[5] a German physician, is equally pronounced in his opinion as to the value of iodine in periodic fevers, and similar favorable reports have been made by several other observers.[1]

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[1] Dr. E. Burdel, Physician to the hospital at Virgon. London Med. Record, May 13, 1874.

[2] Drs. Kleinecke and Hinckey, St. Louis Clin. Record, June, 1882.

[3] Maryland Med. Journal, Feb. 15, 1882.

[4] Braithwaite's Retrospect, 1883.

[5] Virchow's Archiv, xlvii., p. 243.

The experience of Bannergee[2] is extremely interesting, and perhaps throws some light upon the reason for the contradictory results obtained by different observers with this and other remedies which have been recommended for the cure of intermittent fever. This author resorted to the use of iodine in eight cases, in 1878, with but a single successful result. In 1879 it was used in 500 cases, and ninety per cent. of these were reported cured. In 1880 it was again used in 160 cases, but with indifferent success. "*He now recognized that many of these fevers were of an ephemeral character*, and tended to limit themselves, and arrived at the conclusion that about twenty per cent. of cases are cured spontaneously either on the third, fourth, or fifth day, or sometimes even on the seventh or eighth day. He concludes that iodine is much inferior in the treatment of these maladies to quinine"

We quote from a valuable paper[3] upon "Iodine in Malarial Fevers," by Drs. Atkinson and Woods, of Baltimore. These gentlemen, attracted by the testimony in favor of iodine, attempted to determine its real value, under circumstances which they considered exceptionally favorable. Their cases, treated in the Bayview Asylum, Baltimore, came under their observation in July, August, September, and October, 1882, and consisted mainly of foreign laborers who had contracted their fevers while employed in fruit and vegetable canning establishments in highly malarious sections of the neighboring country. In all 76 cases of intermittent and remittent fever were treated, "and their appended histories, with the carefully recorded reports of the effects of treatment, clearly demonstrate the very feeble influence of iodine over malarial diseases; at least over the acute forms." The dose given was usually thirty drops (fifteen minims) of the officinal tincture four times daily. The plan adopted was to give iodine in this dose for five days, and if at the end of that period a cure had not been effected to substitute the sulphate of cinchonidia. The final conclusions reached are as follows:

1. In intermittent fevers it has some feeble influence in controlling the paroxysms.
2. It takes usually from three to eight days to exercise this influence.
3. In *cures effected* there is great danger of a relapse, certainly as great as with Peruvian bark.
4. It is certain to add to any existing diarrhœa or nausea, and is liable to cause each, if they do not already exist.
5. In *remittents*, its effect, if any, is seen in a slow and gradual reduction of temperature, and this reduction is liable to sudden interruptions.
6. In *both forms* of malarial fever it is infinitely inferior to either cinchonidia or quinine: certainly as regards the immediate control of the fever, and, so far as we were able to judge, as regards relapses also.
7. From an economic point of view, the slowness and uncertainty of its action make its use in *hospital* practice fully as expensive as Peruvian bark.
8. There seems to be some ground to believe that it can cause albuminuria.
9. In the large majority of cases of ordinary acute malarial poisoning it has no influence whatever.

We are not prepared to receive this as a final verdict with reference to the value of this remedy, for which so much has been claimed; but we must remark that in therapeutics negative evidence in a considerable number of carefully observed cases must be accorded considerable weight; while, from a variety of reasons, which it is not necessary to specify, positive evidence, apparently of the most definite character, often proves to have no substantial foundation.

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[1] Sircar, in Indian Med. Gaz.; Gibbons, in Pacific Med. & Surg. Journal, Sept., 1880; Geoghan, in Albany Med. Annals, 1880; Wadsworth, in N. Y. Med. Journ., 1879, p. 493, and others.

[2] Calcutta Med. Gaz., Jan., 1882.

[3] Am. J. M. Sc., Phila., July, 1883, p. 64.

Carbolic acid has been vaunted as a specific for malarial diseases, and there is some evidence in favor of its value. But the value of this evidence is a question which it is hard to determine, in the absence of extended comparative tests, made with scientific exactness and impartiality. The history of medicine shows that the ruling medical theory largely controls therapeutics, and it is not difficult to obtain evidence in favor of almost any remedy which may be suggested, especially if its supposed mode of action accords with the experimenter's views relating to the etiology of the disease he proposes to cure. Whatever may be the true value of the medicine under consideration, it is safe to say that the extravagant claims of Déclat and others are not supported by the trials which have been made by unprejudiced observers. Dr. Curschmann,[1] of Berlin, after numerous trials with large doses, reports the remedy worthless.

Surgeon McNally, of the Indian Medical Service, made a trial of carbolic acid in the treatment of uncomplicated intermittent fever at Secunderabad, where the disease prevailed extensively among the soldiers of the Third Regiment. He reports as follows:

> These trials prove at least that carbolic acid is much inferior to any of the other remedies employed. It is now my belief that this medicine is of *no value whatever in the treatment of intermittent fever*, and that the patients would have got well as soon with the usual aid of a purgative, rest, and a blanket. In some cases (not recorded) a few doses of quinia or of quinidia were sufficient for cure after the marked failure of carbolic acid. I am not in a position to speak positively with regard to the reputed diaphoretic action of carbolic acid, but I think it is very doubtful. Abundant diaphoresis certainly did occur in the patients who were taking it, but also occurred in the patients who were not. Irritability of stomach was a common accompaniment of the fever which prevailed in this corps during the past year; and, contrary to what might be expected, carbolic acid did not seem to alleviate it in any case. These observations are, I think, sufficient to establish that carbolic acid cannot be relied upon in the general treatment of ague, and that its value in any case is, to say the least, exceedingly problematical.[2]

Unfavorable reports have also been made by Caisne, Marken, Eisenlohr, and others (Hertz). On the other hand some of those who first tried the drug gave a favorable report as to its value. Thus Treuliche (1871) found that it promptly and permanently arrested intermittent fever in cases in which quinine had failed; and Barrant and Tessier (1869) reported that in their hands it was effectual in arresting intermittent fever at Mauritius. It was administered by the stomach in the dose of one grain of pure acid in an ounce of water, or bitter infusion, three times a day; or by hypodermic injection—64 gr. of acid to 4 oz. of water, and 12 to 30 minims of this solution for a single injection. Treuliche gave as much as 4⅛ gr. in an infusion of gentian, three times daily.

Another remedy, which when first proposed received a considerable amount of favorable endorsement, but which has not come into general use, is the *hyposulphite of soda*. This was first recommended upon theoretical grounds in 1864, by an Italian physician, Dr. Giovanni Polli. The conclusions reached by Dr. Polli himself, after seven years' trial of the sulphites, are summarized as follows:

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[1] Centralblatt, Sept. 6, 1873.

[2] Indian Med. Gaz., April 1, 1874.

1. That marsh fever can be cured by the sulphites alone. 2. That the action of the sulphites is less rapid on the attack of the fever than the sulphate of quinia; they do not stop so suddenly the periodical course of the fever, but they usually gradually diminish the violence of the symptoms, till they disappear altogether. 3. That the sulphites, *en revanche*, act much more certainly in preventing the return of the fever than quinia. Among 403 cases treated by the sulphites relapses only occurred in 5.7 per cent., while in 183 cases treated with sulphate of quinia the relapses amounted to 44.5 per cent. 4. That many cases of miasmatic fever, long rebellious under treatment by quinia, were cured by the sulphites alone. 5. That the sulphites can be employed with success even as a prophylactic means, and that they may be thus used for long periods without danger, which is not the case with the preparations of quinia. 6. That the sulphites can be administered without danger in spite of concomitant gastro-intestinal irritation and during the attack, and finally that many sequelæ of fever (excepting always anæmia) may be very advantageously treated with the sulphites. The *curative* treatment adopted by M. Polli is given in the following prescriptions. If sulphite of soda be used, the proportion is 20 grammes of the salt in 200 of water, sweetened with honey or some aromatic syrup. This quantity is given in the course of twenty-four hours in divided doses. When the sulphite of magnesia is prescribed, he gives 12 grammes in the same quantity of water, taken in four or six doses; when the hyposulphite of soda, 15 grammes in 300 of water, taken in a similar manner. It is essential to take the remedy one hour before or two hours after a meal, and not to drink, except after a long interval, any acid substance, such as lemonade, or to take acid fruits or vinegar.[1]

Favorable reports with reference to the value of the sulphites in the treatment of intermittent fever have been made by a number of American physicians. Dr. W. E. Turner,[2] of Leavenworth, Kan., reports that he used the hyposulphite and sulphite of soda in over 125 cases with almost unvarying success. Dr. Baxter, of Moscow, Ia., treated "over one hundred cases of simple intermittent and remittent fever with this remedy alone, and in no case has there been an exacerbation *after taking the remedy a reasonable length of time.*"[3] Dr. S. E. Hampton[4] states that of 66 cases in which this remedy was used it was successful in all but one. Dr. J. P. Little, of Richmond, Va., says:

For some four years past I have been using the hyposulphite and also the bisulphite of soda as a substitute for quinia in the treatment of intermittent and remittent fevers.

It was first used as a febrifuge in measles, scarlet fever, and similar affections; accidentally its value in fevers of a malarious origin was discovered, and I at once gave it a thorough trial.

Intermittent forms of fever prevailed very extensively immediately after the war; and as quinia generally failed to give relief, I made free and frequent use of this remedy and with marked good effect.

I have used it in my own case; quinia had failed in removing my fever, although it had succeeded in producing an intense headache; the hyposulphite speedily relieved me.

For an adult the dose is from ten to twenty grains every three or four hours. I have given thirty grains every two hours in cases of high fever. Dissolve each dose in a wineglassful of water. As it is a mild laxative there is no necessity for the use of purgative medicine. Of the two salts, I consider the bisulphite the better in its effects.[5]

This report seems to us to be especially instructive and to furnish a clue which may reconcile the contradictory reports with reference to the value of this and other proposed remedies for *malarial* fevers. We have evidence that iodine, carbolic acid, and the sulphites will cure malarial fevers. These are all recognized as valuable antiseptic agents and we might expect them to give good results in that form of intermittent fever —pseudo-malarial fever—which results from septic poisoning. We are convinced that much of the "malaria," of which we hear so much in large cities is of this character, and quinine does not seem to be the specific for malarial fevers of this kind that it is everywhere recognized to be for malarial fevers properly so-called—paludal or telluric. We read in the above quotation that the "intermittent forms of fever" which were cured by hyposulphite of soda, were not cured by quinine, "which generally failed to give relief." Evidently then they differed essentially from paludal intermittents, which are cured by quinine. Again, it is said that these intermittent forms of fever "prevailed very extensively immediately after the war." What a significant fact! For four years Richmond and vicinity had been a great military camp, and the conditions had been most favorable for the accumulation upon the surface, or at least in the superficial layers of the soil, of that kind of organic material which produces the malarial fever peculiar to large cities and to large armies, which has been very aptly called fæco-malarial fever, and against which quinine is not a specific.

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[1] From The Practitioner, Dec., 1871.

[2] Leavenworth Medical Herald, Nov., 1867.

[3] Am. J. M. Sc., Phila., Oct., 1866.

[4] Cincinnati Lancet & Observer, Nov., 1867.

[5] Am. J. M. Sc., Phila., Jan., 1870.

According to Hertz, Griesinger and other German physicians have been unable to obtain any favorable results from the use of the sulphites in malarial fevers. A negative result is also reported by Dr. Wm. G. Chandler, who tested the sulphites of soda, and of ammonia, in twenty cases of intermittent fever in the service of Dr. Austin Flint, in the wards of Bellevue Hospital, New York. This report is especially valuable as the cases are reported in full. The following is a summary statement of the results and conclusions reached:

Number of cases cured	2
" " improved	4
" " neither cured nor improved	14
Total	20

> In crediting the sulphites with two cures we have perhaps acted generously rather than justly. The tendency of intermittent fever to self-limitation, and the benefit produced in all cases by improved diet and a change of air, have not been forgotten, but we desired to represent the case as favorably as possible, and give the sulphites credit for all that they could do. And this is all that the sulphite can accomplish. But an agent which can cure only one case of intermittent fever out of ten will not come into very general use at present.
>
> The following conclusions are drawn from the above cases:
>
> 1. That in a few cases the paroxysms of intermittent fever are relieved and possibly arrested by the sulphite of soda or sulphite of ammonia.
> 2. That in the large majority of cases these remedies fail entirely to arrest the paroxysms, or to lessen either their severity or frequency.
> 3. That these remedies require to be given in large doses for a length of time to effect any appreciable improvement.
> 4. That, when given in doses sufficient to modify or arrest the paroxysms, they produce considerable irritation of the stomach and intestinal canal.
> 5. That as remedies for intermittent fever they are in every respect vastly inferior to quinine.[1]

Another remedy which has been recently proposed for the cure of intermittent fever is *resorcin*, which has been called "poor man's quinine." It is said by Ugo Bassi[2] to be but little inferior to quinine, and out of twenty cases treated, sixteen were permanently cured. We can only say, with reference to this remedy, that more extended experience is required in order to test its real value.

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[1] The Medical Record, New York, Dec., 1868.

[2] Gaz. Med. Ital., Prov. Venet., 1883.

The mineral acids, and especially *nitric acid*, have been proposed as antiperiodic remedies. Dr. E. S. Baily, of Indiana, is said to have first recommended nitric acid for this purpose, and Dr. Wm. A. Hammond has given evidence in favor of its value. While on duty as a medical officer of the army at Fort Riley, Kansas, Dr. Hammond prescribed nitric acid for 32 cases of quotidian and tertian intermittent; nine other cases were treated with the sulphate of quinine. "Of the cases cured by nitric acid, three had previously used quinine without effect, and of those in which quinine had proved successful nitric acid had been employed without benefit in two, and in one other had to be omitted on account of causing nausea, heartburn, etc." The average period of treatment before the disease was permanently arrested was the same with each remedy—three days.[1] The acid was given in ten-drop doses, largely diluted with water, three times daily.

Senator[2] has reported cases of intermittent fever cured by the administration of *salicylic acid*, one or two doses of one to two grammes being given in warm water and glycerine shortly before an expected paroxysm—2 parts of salicylic acid; 200 parts of warm water; and glycerine q. s. to dissolve.

Picric acid has been recommended by Dr. Aspland,[3] in old cases where quinine has lost its effect by continuous usage.

According to Moxon[4] the *bromide of potassium* will cure ague, especially in persons who have removed from the malarious locality where it was contracted.

Chloride of sodium, in the dose of from ʒ ji. to ℥ ss. twice a day has been recommended by Piorry, Thomas, Pioch, and others as an effectual remedy for ague.

M. Colin reports that he has had good results, especially in obstinate quartans which have not yielded to the administration of quinine, from the use of *ammonium acetate*, used in conjunction with warm drinks. From 15 to 20 grammes of the salt are given in solution about two hours before the expected return of the paroxysm.

Black pepper was a favorite remedy with the ancients, and at the present day *piperine* is frequently prescribed with advantage in combination with quinine, especially in the treatment of old cases. Hertz considers this the most effective vegetable remedy after the cinchona alkaloids. It may be given to the extent of ten to fifteen grains during the intermission.

The *sulphate of biberine* has been offered as a substitute for quinine. Professor Maclean reports that he has given it an extensive and careful trial, and has found it useless in the treatment of all forms of intermittent fever.[5] He has also tried the tincture of barberry, which is an old remedy in ague, and thinks it may possess some power as a febrifuge, but says: "It is so uncertain in its action, so immeasurably inferior to quinine, that, in my judgment, to use barberry when quinine is available, is to trifle with the constitutions of our patients" (*loc. cit.*). We believe that this remark is equally applicable to several other reputed remedies in our list.

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[1] Maryland & Va. Med. Journ., Feb., 1861.

[2] Centralblatt, No. 18, 1875.

[3] British Med. Journ., Nov. 2, 1867.

[4] Braithwaite's Retrospect, Part lxii., p. 33.

[5] Reynolds' System of Medicine, vol. i., p. 65.

Dr. W. G. Carter,[1] of Virginia, prefers *sulphate of zinc* to quinine for the cure of ague and fever.

De Renzi[2] cures intermittent fever by the use of electricity. He says that in the majority of cases this remedy arrests the fever more promptly than quinine. He uses the constant and faradic currents, and considers the latter the most efficacious. It is to be used for half an hour, of medium intensity, the patient holding a rheophore in each hand.

Fleury has claimed that we have a substitute for quinine in cold water, used as a douche (54° to 57° Fahr.) one or two hours before the attack (Hertz).

Willow leaves (*Salix Babylonica*, or "weeping willow," and *Salix Egyptiaca*) are said to be an ancient remedy in India. In old cases where there is gastric irritability, this remedy is said by Surgeon Chetau Shah, of Cabul, to be superior to quinine.[3]

Dr. Segur, of Porto Rico, has used *coffee* with the happiest effect in cutting short an attack of intermittent fever. If properly managed, he considers it better in many cases than sulphate of quinine.[4]

Dr. Richard Newton,[5] Assistant Surgeon U. S. A., has recently recommended *conium* in combination with quinine and peroxide of iron as a useful remedy in intermittent fever.

The *ethereal oil of mustard*, in doses of two or three drops in a ten per cent. alcoholic solution, or in a large quantity of boiled water, is said by Tabercorn[6] to have given brilliant results in many cases of malignant malarial fever treated by him in Moldavia.

The peasantry in Russia are said to cure themselves of intermittent fever by the use of urine as a medicine. Acting upon this hint Dr. Belvousoff[7] has tested carbamide, or *urea*, and finds that it acts as a specific and for several reasons is preferable to quinine.

Quite recently another specific, which is also successful when quinine has failed, has been recommended by Dr. Maglieri.[8] This consists in the use of a decoction prepared from a fresh lemon, cut into small pieces.

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[1] Southern Clinic, June, 1879.

[2] Annali Univer. di Med., 1883.

[3] Indian Med. Gaz.

[4] Gaillard's Med. Journ., June, 1881, p. 543.

[5] The Medical Record, Jan. 19, 1884.

[6] Meditz. Obozrenie, Feb., 1880.

[7] Scientific American, Feb., 10, 1883.

[8] Bull. Gén. de Thérap., July 30, 1883.

CHAPTER IX.

CONTINUED MALARIAL FEVERS.

THE most prominent character of malarial fevers, properly so-called, is the periodic tendency of the pyretic movement. This has been prominently brought to view in our account of "Malarial Intermittent Fever." The same periodic tendency is manifested in *uncomplicated* continued malarial fevers, which are accordingly commonly known as "remittent" fevers. The term "periodic fever" is also frequently used as synonymous with malarial fever; and Bartlett, in his classical "Treatise on Fevers," uses the heading "Periodical Fever" to include all the recognized forms of malarial fever. A remittent is a continued fever, no matter how well-marked the periodic exacerbations and remissions of the febrile movement may be; for if there be a complete apyretic interval, the case must be classed as one of intermittent fever.

Moreover, a remittent character is not peculiar to continued fevers of malarial origin. We see it also in enteric fever, in acute tuberculosis, and to some extent in febrile diseases generally. On the other hand forms of fever occur, especially in tropical regions, which are ascribed to the action of the malarial poison by distinguished medical authors who have had personal opportunities for observing them, in which this periodic tendency is very obscure or altogether wanting. We have therefore thought best to include all malarial fevers not distinctly intermittent in character under the general heading "Continued Malarial Fevers." But it must be understood that we recognize marked periodicity in the febrile movement as the most prominent distinguishing characteristic of this class of fevers; and the well-known "remittent fever," which occurs side by side with intermittent in the malarious sections of the United States, as the leading or typical form of continued malarial fever.

Dr. S. M. Bemiss, in a clinical lecture on "Malarial Remittent Fever," delivered at the Charity Hospital, New Orleans, says: "I ask your attention to-day to a case of continued malarial or remittent fever. . . . Its nosological classification is better expressed by the adjective '*remittent*' than by 'continued,' but if you carefully examine the charts of temperature which are being passed around, you will observe the striking parallelism between them and the temperature charts of typhoid fever so lately exhibited to you. You perceive, also, that while the charts show marked remissions, there is no decline of temperature to the normal standard until in the course of convalescence the remittent form of fever lapses into the intermittent type."[1]

Trousseau says: "How have the followers of nosography been able to deceive themselves so long? Did they not admit in 1821 that intermittent fevers sometimes passed to the remittent type, without being the less susceptible to cure by cinchona? What, in truth, is a remittent fever, even as regarded by the superficial pyretology of the school, except a continued fever? Is not the febrile state continuous? And what matter that it has remissions and exacerbations, if, as everybody admits, the continuous fever is a conventional type? And if remittent fevers *à quinquina*" (curable by quinine) "differ from the continued non-miasmatic fevers as much as gout differs from scrofula, it is certainly in points of very different importance to that of type. We do not deny the existence of such points, but we deny them the first rank, which we wish to see filled by more fundamental nosological conditions, more akin to the therapeutic indications."[1]

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[1] The Medical News, Phila., March 24, 1883.

On another page Trousseau remarks: "The type is not the disease; for all diseases are susceptible of assuming the same type. Conversely, the most various types may be symptomatic of the same disease, in one or in different patients. The type, be it intermittent or periodic, belongs essentially to the organism, and not to the external cause which acts upon it."

We believe that there is profound wisdom in these remarks, and that in giving an amount of attention to types of morbid manifestation not justified by the relative unimportance of these phenomena relating to the individual—to the mode of reaction of the nervous system to the toxic agent—many authors have overlooked essential and fundamental etiological distinctions. As regards "remittent fevers," we are inclined to exclaim with Dutroulau, "*C'est le chaos.*"

We cannot hope to bring order out of chaos by our feeble efforts, but a step will have been made in the right direction if we succeed in convincing practitioners in our own country that the remittent type is not necessarily evidence of malarial poisoning, and that the heading "Remittent Fever" is not broad enough to include all the different forms of disease which have a remittent type, unless we are willing to cast aside etiological distinctions and those furnished by therapeutics. It is notorious that certain cases called "remittent fever" run a protracted course, and are not abridged by the administration of quinine; that other forms of "remittent fever" have a tendency to terminate by sudden defervescence on the third or fifth day (Maury) independently of the administration of quinine; and that still other cases have a tendency to run into the intermittent form unless cut short by the administration of quinine. These last are evidently the most closely allied to malarial intermittent, and without doubt have the same etiology. As regards the other forms referred to there is room for much doubt. A recent writer, Guéguen,[2] makes a distinction between the fever which we shall describe as *simple malarial remittent fever*, and "bilious remittent fever," which in this country are commonly assumed to be one and the same disease. Our simple remittent, which corresponds with the "ordinary remittent fever" of Morehead, and the "paludal remittent" of other authors, is called by this author "fièvre rémittente quotidienne," and he recognizes two forms of "bilious remittent fever," which he believes to be quite distinct from it in their clinical history and in the character of the pyrexia, if not in etiology. We shall not follow this author in the attempt to divorce simple remittent fever and bilious remittent fever, but confess that we see some ground for making the distinction.

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[1] Treatise on Therapeutics, Am. ed., vol. iii., p. 165.

[2] A. Guéguen, Aide-Major au 2e régiment d'infanterie de marine. Étude sur la marche de la température dans les fièvres intermittentes et les fièvres éphémères. Paris, 1878.

We trust that no misconception will arise from our use of the word *continued* at the head of this article to indicate that the fevers under consideration are not intermittent. This term has been very generally employed by medical writers as opposed to remittent, and to indicate that the febrile movement is continuous, *i. e.*, uniform in its course. Thus a remittent fever is said to assume a continued form when remissions can no longer be detected. The word is also used in this sense in the present volume, but in that case, instead of saying "continued malarial fever," we would place the adjective continued immediately before the noun, and say, a malarial continued fever.

Simple Malarial Remittent Fever.

Definition.—A paroxysmal fever of malarial origin, which differs from malarial intermittent fever mainly in the fact that the hot stage is more prolonged, and is not followed by an interval of complete apyrexia; and that the cold stage is commonly ill-defined or entirely absent, except at the outset. In severe cases gastric irritability and bilious vomiting are common symptoms.

Synonyms.—Ordinary remittent fever; *fièvre rémittente quotidienne;* paludal remittent; bilious fever; bilious remittent fever; jungle fever; coast fever; country fever; marsh fever, etc.

The dividing line between quotidian intermittent and simple remittent is an arbitrary one, for they are in fact but different forms of the same disease and often pass insensibly one into the other. Wood says:

> The two affections sometimes approach each other so closely in form that it may be impossible, in relation to a particular case, to decide to which of them it belongs. In intermittents there is often some degree of morbid action between the paroxysms, and in remittents often very little; and it is not always possible to determine whether the morbid action that exists does or does not amount to fever. If it be pronounced not to be fever, the disease must be considered intermittent; if fever, remittent. In the latter affection there is every grade, from the doubtful form just alluded to up to an almost uniform continuous fever.[1]

Since this was written by the distinguished author quoted we have learned to use the clinical thermometer, and applying the rule laid down we may say definitely, this case is intermittent, for the temperature fell to the normal point between two febrile paroxysms, and this is remittent, for it remained a half degree, or a degree, above the normal during the period of remission. It will be admitted that such a distinction can only be justified on the score of convenience of description, and that it has no deeper foundation than the division which Griesinger makes of remittent and continued fevers into those of *light, heavier, and highest grades;* a division which Hertz says "finds its justification in the fact that it isolates certain pictures of disease and facilitates our study of their features."

We do not think it necessary to follow Griesinger in this division of remittent fever into three grades, but prefer to consider the different clinical varieties of this fever with reference to the prominent symptoms, or complications, which give a special character to the clinical picture. We can see no objection to this course, which has been adopted by some of the best clinical teachers—Morehead, for example—and we think the division into gastric remittents, congestive remittents, pernicious remittents, etc., quite as justifiable for descriptive purposes, and more convenient than that adopted by Griesinger.

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[1] Op. cit., vol. i., p. 277.

Simple remittent fever, then, as here described, corresponds with the *first grade* of Griesinger, or with the "ordinary remittent fever" of Morehead. It is the common form of continued malarial fever, in the United States and elsewhere, in those localities where the conditions are most favorable for the development of malaria, and where typical intermittents are most prevalent.

Etiology.—It is commonly assumed that the remittent form is due to great intensity or concentration of the malarial poison, and there is little doubt that this is true in a general way as regards simple remittent and pernicious remittent fevers. But it is also true that the development and degree of severity is largely influenced by secondary causes, and especially in the "inflammatory"—ardent—and complicated forms of the disease. These secondary causes relate both to the individual and to his environment. Thus, of two individuals exposed under precisely the same circumstances, one may have a quotidian or tertian intermittent, and the other a remittent attack. Again, in the case of two individuals in equal health and exposed under similar circumstances, one may escape entirely and the other may suffer an attack of remittent fever as the direct result of a debauch, of excessive fatigue, or of exposure to the direct rays of the sun. Heat is very generally recognized as a potent exciting cause, and no doubt Professor Maclean is quite right in saying that remittent fever is most prevalent and fatal when high temperature and malaria act together. But that climatic causes alone are sufficient to account for the occurrence of these fevers is easily disproved, and we cannot do better than to quote the language of Professor Wood to show that this hypothesis is untenable:

> The essential cause of bilious remittent is probably the miasma which proceeds from marshes, etc. Many believe that, while produced by this cause, it may also proceed from others, especially a high degree of heat combined with moisture. If this were the case, why should we not see it originating in the midst of our cities, where the heat is intense and moisture often abundant? Why does it not occur constantly among seamen navigating equatorial seas, whether long from port or not? The fact is well known that the crews of ships within the tropics remain free from the disease so long as they keep at a certain distance from the shore. They may be affected with scurvy, dysentery, diarrhœa, and various phlegmasiæ; but they escape bilious fever. Let them, however, approach a miasmatic coast, and it often happens that almost the whole crew are seized with the disease.[1]

The commonly accepted view that the remittent form is evidence of greater intensity of action of the morbific agent does not meet with universal acceptance, and while admitting that malaria is an essential factor in the production of these fevers as well as of those of intermittent type, the continued character of the pyretic movement is ascribed by some authors to causes quite independent of the quantity or intensity of the toxic agent. This is the view of M. Colin, who believes that continued forms predominate over intermittents "less from the intensity of action of the miasm than from two influences of quite a different order; on the one hand the external temperature, and on the other the date of intoxication." According to this author, remittent and continued fevers are in nearly all malarious regions the initial form of febrile manifestation. He says: "In Rome this rule was so absolute that among those attacked with tertian or quotidian intermittent in September or October, I have not found one out of ten who had not had previously, in July or August of the same year or of preceding years, an attack of remittent or continued fever."

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[1] Op. cit., vol. i., p. 288.

M. Colin further says: "But not only is remittent or continued fever proper to individuals who are attacked for the first time: it also presents the important and unique character of never, or almost never, recurring in the same individual. An individual may be seized at any moment, from the most trifling cause, with periodic fevers—quotidian, tertian, etc.—he will have but once *la fièvre chaude ;* or rather the relapse of this is marked by an attack of intermittent fever, in conformity with the law which we have above stated, of the transformation of continued into periodic forms, by the fact of their succession in the same individual."

These views of M. Colin receive strong support from the facts advanced by himself and the quotations made from various authorities, and demand careful consideration. But malarial remittent fever in the United States does not, so far as we have been able to ascertain, conform with the law laid down by this author; and we must suppose either (*a*) that he is mistaken, or (*b*) that the continued malarial fevers to which he refers differ essentially from the continued fevers of malarial origin (simple remittents) in this country, or (*c*) that our medical authors and experienced practitioners have overlooked a very important fact in the history of malarial fevers, viz., that remittent fever is the initial form and does not recur in the same individual.

As this is a very important and interesting subject, and one which, so far as we know, has not received special attention at the hands of medical authors in this country, we shall consider it at some length. Colin quotes from numerous authors in support of his position. From these quotations we select the following:

> Dr. James Raynald Martin says: "The Europeans who come to reside in malarial districts are attacked with continued and remittent fevers, then with intermittents."[1]
>
> We read in Griesinger: "While the natives or acclimated individuals of the marshy coasts in the tropics seem to suffer only from intermittent fever, the newly arrived, and in certain localities all the newly arrived without exception, are attacked by grave forms of remittent fever."

Evidence to the same effect is given by numerous authors with reference to first attacks of fever among unacclimated strangers soon after their arrival in certain tropical regions; but we are not prepared to admit that these "remittent or continued" fevers of the tropics which do not recur in the same individual are identical with the endemic remittent fever which prevails so extensively in the southern portions of our own country side by side with intermittent fever, and from which, if we are correctly informed, the permanent residents of malarial localities enjoy no exemption. We quite agree with Hertz that "not all those diseases which are regarded as remittent or continued malarial fevers, in the tropics, or in more northern malarial districts, could maintain their claim to this title if subjected to the test of scientific criticism." This author further says: "Even the physicians of our own lands are too liable to designate as malarial diseases attacks of pneumonia accompanied with jaundice, or simple gastric disturbances with or without jaundice, or mild grades of typhoid fever running an irregular course."

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[1] The Influence of Tropical Climates, p. 185.

There can be no doubt, also, that the "grave forms of remittent fever" which, according to Griesinger, attack all the newly arrived without exception in certain tropical localities upon marshy coasts, have been, in some instances at least, nothing more nor less than yellow fever.

In view of the great confusion which exists at present in tropical regions with reference to the differential diagnosis of fevers, and the undoubted influence of an elevated temperature in modifying the course of fevers due to a specific cause, we think it right to demand that M. Colin's views be tested in the light of facts relating to the history of simple remittent fever as it prevails in temperate regions, rather than by observations made in the tropics and especially by those recorded by the older authors. For it is only recently that English physicians in India have recognized the extended prevalence of enteric fever in that country,[1] and no one at the present day, reading the accounts of the "malignant" and "pernicious" malarial fevers given by some of the most celebrated authors of the last century or the beginning of this, can doubt that in many cases specific yellow fever was encountered without being recognized.

M. Colin himself recognizes the factor heat as an essential one in the development of the annual "endemo-epidemic" of remittent fever observed by him during the French occupation of Rome, and says that this occurred before the conditions most favorable for the evolution of malaria were in full force. He thus takes away much of the force of the argument he has made in favor of the view that first attacks of malarial fever have a tendency to assume a continued form. We have ample evidence that newcomers in hot climates are more susceptible to thermic fever than the natives. Fayrer says: "It is well known that a native can bear an amount of sun on his bare head and naked body with indifference that would prostrate a European." Our view of the case is that sthenic unacclimated strangers suffer more frequently from remittent fever in Rome and elsewhere, not because this is a primary form of malarial fever, but because they are more susceptible to the influence of the second factor—heat—which plays an important part in the development of these fevers, and especially of the varieties known as "inflammatory remittent," "gastric remittent," and "congestive remittent," of which we shall have occasion to speak hereafter. We believe that this factor has much less to do with the simple remittent fever of temperate latitudes, in which the remissions are generally well defined, and which are far more amenable to the specific action of quinine than the other varieties named.

The view which Colin has supported at considerable length in his valuable work, although it seems to have been original with him, had been previously advanced by American authors. Thus Dr. George B. Wood says:

> Persons who dwell in miasmatic districts are less susceptible to the disease than strangers who incidentally visit them: and after complete recovery from one attack of remittent fever the visitor acquires, in a certain degree, the same comparative insusceptibility, or in other words, becomes in some measure acclimated.[2]

Dr. Stephen Rogers,[3] who as surgeon to the Panama Railroad Company had abundant opportunities for studying malarial diseases upon the Isthmus of Panama, gives to the fever which attacks the unacclimated in tropical regions the name of "first miasmatic fever," and says of it:

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[1] See Fayrer, op. cit., pp. 164–228.

[2] Op. cit., vol. i., p. 289.

[3] Quinine as a Prophylactic or Protective from Miasmatic Poisoning, a Preventive of Paroxysms of Miasmatic Diseases, together with some Remarks upon its Use in the Treatment of Developed Miasmatic Diseases. By Stephen Rogers, M.D., U.S.A., for-

> The law relating to this fever is similar to or identical with that observed by yellow fever in localities where it is an annual endemic, viz., the longer one resides, under any circumstances, in the locality where it is suffered, the less liable he becomes to its attacks.
>
> A species of toleration of the surrounding influences is acquired, lessening the impression of the poison upon the sensorium; so that after more or less time, aided perhaps by a depression of the powers of life and consequent want of vital force to sustain a violent contest, the intense and destructive character of the fever ceases to occur, except in the rare cases just alluded to.

The statistical data relating to the prevalence of remittent fever in our armies during the war (see page 90) seem to support M. Colin's view, inasmuch as they show that remittent fever was more prevalent and more fatal among the new levies during the first years of the war than among the seasoned—"acclimated"—troops of a later period. We have, however. given a different interpretation to the facts, and incline to the belief that if these statistics related only to uncomplicated cases of simple remittent fever of malarial origin, they would tell a different story. We would not, however, be too positive in this matter, and commend the question to the attention of those physicians who are located in decidedly malarious regions in this country as one well worthy of their consideration.

Notwithstanding the very positive statement by M. Colin in the text (page 146) that remittent fever does not recur in the same individual—"elle présente en outre ce caractère important et unique, de ne récidiver jamais ou presque jamais"—he shows in a foot-note that this rule is far from being absolute either in Rome or in Algeria.[1] That it is still less a law in this country is established by the uniform testimony of a number of prominent and experienced physicians in the South, who have kindly responded to the writer's inquiry with reference to this alleged immunity as a result of a single attack.

Dr. Jerome Cochran, of Alabama, writes me as follows:

> MONTGOMERY, ALA., January 29, 1884.
>
> In reply to yours of the 14th, I promised to bring Léon Colin's statement before the Montgomery Medical Society, the older members of which have had an immense experience with remittent fever. The President of that society writes me under date January 29th as follows: "The unanimous verdict of the members present was that the statement of Léon Colin is not true.[2] They claim to have seen numerous instances in which remittent fever has occurred more than once in the same individual, and seemed inclined to the opinion that it might so occur an indefinite number of times."

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merly Assistant Physician to the Island Hospital, New York, and Surgeon to the Panama Railroad Company, Licentiate of the Royal University of Havana, Cuba, etc., Surgeon of the Seventh New York Regiment 8vo., pp. 24. 1862.

[1] In 1865 there were received into the military hospitals of Algiers 3,199 cases of remittent fever, of which 359 (one-ninth) were second attacks—*par récidives*. The same year, out of 15,080 cases of intermittent 4,276 were cases of relapse (about one-fourth). During the same year in Rome 449 cases of remittent fever were received into the military hospital at Rome, only 18 of which (1 in 25) were second attacks, while out of 1,682 admissions for intermittent fever there were 322 (1 in 5) who had previously suffered an attack (op. cit., p. 146).

[2] This denial refers, of course, to remittent fever as observed in Alabama, and not to the statements of M. Colin with reference to remittent fever as observed by him in Rome and elsewhere.

Dr. F. Peyre Porcher, of Charleston, S. C., writes me as follows:

> At a meeting of the medical society held last evening, it was the united opinion of eight or ten physicians present that remittent fever often returned, and sometimes recurred the same season. Several of the gentlemen stated that they knew examples of what is called "bilious remittent" occurring in the same subject two or three summers in succession. There were only a few who could assert that they had met cases recurring the same season. If a year elapses before a new attack, there might of course have been a fresh exposure to malaria.

Dr. Porcher also kindly obtained for me the evidence of several practitioners residing in country towns in South Carolina. This was to the same effect. Dr. Evans, of Florence, says:

> In my experience second attacks of remittent do occur in the same individual. I had one case the past summer where the attacks occurred three times and continued nine or ten days each time. . . . In the case mentioned above the attacks were separated by intervals of fourteen to twenty one days.

Dr. Otis F. Manson, of Richmond, Va., says:

> In this climate, in the large proportion of cases the first attacks are of remittent type, and when relapsing assume an intermittent form; but it is not unusual for relapses of remittent to assume the remittent type again. I have seen hundreds of cases of relapse of malarial remittent fever reappearing in the remittent form, sometimes five or six times in the same person. According to my observation on the James and Roanoke Rivers, when violent epidemics occur the cases are generally remittent at first and finally subside, in the most of the cases, into the intermittent type. The pernicious form, which M. Colin admits frequently relapses, is usually of remittent type.

Dr. Stanford E. Chaillé, of New Orleans, says:

> My colleagues, Professors Bemiss, Logan, and Elliott, all concur with me that it is not rare that cases of remittent fever recur in the same individual, and that, as in all other forms of malarial fever, one attack predisposes to another.

Dr. G. B. Thornton, who has had an extended experience in the vicinity of Memphis, Tenn., has given me a reply to the same effect.

It is evident that the views of leading practitioners in the malarious regions of the United States are in accord with those of our standard medical authors—Wood, Bartlett, Flint—with reference to the etiology of remittent fever, and these views may be concisely stated in the language of the author last named:

> Between simple remittent and intermittent fever there is a close relationship. These two forms of fever are mutually convertible into each other; they undoubtedly involve the same cause, and they are controlled by the same specific remedies. The propriety of recognizing remittent as distinct from intermittent fever is denied by some writers. Bouilland calls it a "real nosological superfœtation!" There is, however, a practical convenience in considering the two forms as separate affections, admitting that they are essentially identical.[1]

A very different view from this has recently been advanced by Dr. Norman Chevers, an English physician who has had an extended experience in India. Dr. Chevers says:

> Thousands in Lower Bengal have their systems saturated to the very utmost with the poison of intermittent, but never become the subjects of remittent. On the other hand, intermittent is no safeguard against remittent. When a denizen of the marsh ventures into the jungle, he may get remittent, and his disease carefully observed will

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[1] Flint's Practice of Medicine, p. 837.

probably be found to have some resemblance to intermittent. I repeat, remittent is not, in my opinion, modified or aggravated intermittent.[1]

Other writers have referred to a difference in the topographical distribution of intermittents and remittents. Thus Griesinger says that in districts where malaria is endemic the remittent variety prevails in the humid coast regions, and ordinary intermittent on higher lands, "a circumstance which is undoubtedly due to the varied intensity of the morbific agent" (Hertz). This simply corresponds with the well-known fact that in our own country the relative proportion of remittents is greater in southern and intensely malarious regions, than in northern localities, where conditions are less favorable for the evolution of malaria. If it could be shown, however, that remittent fever prevailed endemically within a certain area where intermittent was unknown, we would be forced to the conclusion *that this kind of remittent* differed in etiology from intermittent and from the simple *malarial* remittent fever at present under consideration.

Seasonal Prevalence.—To illustrate the seasonal prevalence of remittent fever in various parts of the United States we give the following table, which is compiled from the data contained in the first medical volume of The "Medical and Surgical History of the War." For this purpose we take the figures relating to a single year only, viz., from July 1, 1864, to June 30, 1865:

Department.	Mean Stren'th	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Ap.	May.	June.
Dep't of the East.....	10,947	27	40	29	14	21	8	13	33	45	40	41	43
Middle Dep't.........	6,801	97	120	74	119	27	11	24	23	59	44	50	30
Dep't of Washington..	27,792	538	304	323	320	264	196	244	138	110	180	411	474
Middle Mil. Division..	47,795	484	682	561	480	473	217	244	201	214	322	302	428
Army of the Potomac.	89,982	1,610	1,478	1,161	971	839	823	818	607	779	708	748	328
Dep't of Virginia.....	40,183	805	417	422	611	252	182	142	141	125	115	212	240
Dep't of No. Carolina.	19,045	71	314	657	597	212	102	80	289	498	542	435	378
Dep't of the South....	10.121	240	111	130	57	61	48	88	85	35	39	107	230
Northern Dep't.......	17,963	138	322	192	276	88	145	91	*488	214	144	91	75
Mil. Div. of the Miss.,													
Part I.......	109,330	1,600	2,378	1,069	764	1,096	1,275	1,231	804	1,362	967	1,561	1,129
Part II.......	89,384	2,159	2,056	1,518	1,012	531	480	783	346	435	760	733	305
Dep't of the Gulf	45,629	948	1,359	779	567	344	293	203	327	314	429	438	939
Dep't of the N'thwest.	7,278	48	53	41	35	18	9	24	28	24	38	53	72
Dep't of the Missouri.	20,298	320	394	412	346	276	182	121	101	136	113	149	141
Dep't of Arkansas....	28,641	951	1,309	946	444	314	164	118	110	141	138	186	241

* The unusual number of cases in February was no doubt due to the arrival of a considerable number of troops from localities farther south.

The seasonal prevalence for the entire territory represented in the above table is shown below by the graphic method. It must be remembered, however, that these figures do not relate alone to simple malarial remittent, but to all the cases under the general heading "Remittent Fever." Without doubt many complicated cases, and many cases of pseudo-malarial fever are included.

The notable increase in the number of cases in July, which attains its maximum in August and rapidly declines in September, corresponds very closely with the annual "endemo-epidemic" observed by M. Colin among the troops in Rome during the French occupation of that city (see p. 240).

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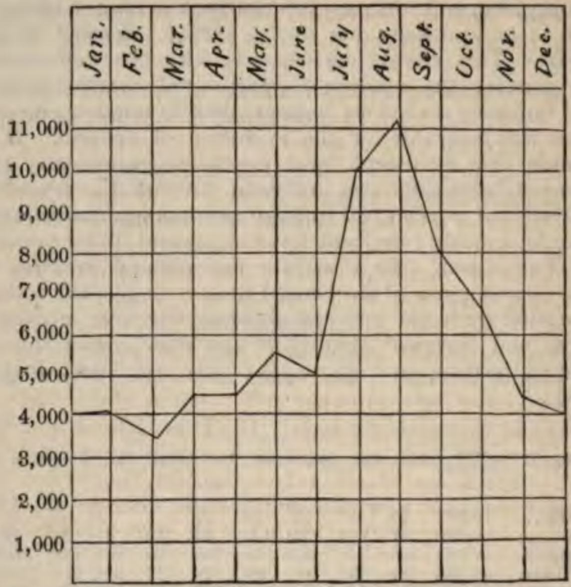
[1] Practical Notes on the Ordinary Diseases of India. Med. Times & Gaz., Lond., Feb. 10, 1883.

But the very considerable number of cases distributed with tolerable uniformity during the remaining months of the year is to the writer an unexpected and surprising fact, and one which we suspect would not be found to correspond with the results of similar statistics relating to *malarial* remittent fever alone.



Graphic Representation of Prevalence of Remittent Fever in the United States.

Chevers says that in India "Paludal Remittent" has its greatest prevalence after the rains in the dry and *cold* season, and no doubt exposure to cold may be an exciting cause, as well as exposure to heat. This is the immediate cause of many cases which occur during the autumn and winter months, and it is well known that relapses frequently occur in the victims of chronic malarial poisoning—more commonly of intermittent, but quite frequently of remittent type—after removal from the malarious region where exposure occurred, as a result of "taking cold."

Period of Incubation.—As in intermittent fever, there is no definite period of incubation in this form of malarial disease. The attack may be developed within a few hours after exposure, or may be postponed to several weeks, or even longer. Wood says: "It is no uncommon event for persons, coming to our northern cities from miasmatic regions, to be attacked with remittent fever in winter, though they may have escaped during the previous summer and autumn. I have repeatedly witnessed such cases among the students of medicine who attend the Philadelphia schools in the winter."[1] Maclean says that, in his experience, from a week to ten days has been the ordinary period of incubation, but he thinks this period is much influenced by temperature—being shorter in hot and longer in cold climates—and by the degree of concentration of the poison. He has given an example of a fatal case developed within a few hours after exposure in a notoriously malarious locality. Fayrer, also, says that "the period of incubation seems to depend upon similar causes to those that determine intensity. Heat and concentration of malarial poison may in certain cases act almost immediately; in others, when there is less activity, a few days to a fortnight or more may elapse." Dr. William P. Buel, surgeon to the Pacific Mail Co. (1856), says with reference to the so-called "Chagres fever," that an incubation period of several days, usually not less than a week, elapses between the time of exposure and that of development.

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[1] Op. cit., vol. i., p. 289.

Modes of Commencement.—An attack of quotidian intermittent may assume the remittent form by a gradual, or abrupt, prolongation of the daily febrile paroxysm to such an extent that there is no longer any apyretic interval. This is quite a common occurrence in those cases due to malarial poisoning alone, whereas in cases developed by the combined action of heat and malaria the febrile movement is commonly remittent or even continuous from the outset. Certain prodromal symptoms frequently precede the development of remittent fever. The patient often has more or less gastric distress, attended with nausea and vomiting; there is loss of appetite, disordered taste, languor, and lassitude; the tongue is apt to be slightly furred, especially posteriorly, and the pulse is increased in frequency by slight exertion. In certain cases the patient complains of a feeling of soreness in the muscles, and there is often slight frontal headache and pain in the lumbar region. Chilly sensations and flashes of heat are also experienced in some cases at a certain hour every day or every second day. Again, the attack may be abrupt, the patient being seized, while in apparent health, with a slight chill, followed by intense febrile reaction, which is commonly attended with severe headache and bilious vomiting.

Types.—Periodic exacerbations and remissions in the pyretic movement occur in this form of malarial fever which correspond with those observed in intermittent; and in many cases a distinct cold, hot, and sweating stage may be recognized. More commonly, however, the cold stage is absent, except at the outset of the attack, and in place of a regular sweating stage the skin simply becomes moist during "the remission," at which time the temperature often approaches the normal, and all the distressing symptoms undergo a marked amelioration. Very close observation is often necessary in order to detect this remission, which in truth is, in many cases, not so much a remission in the febrile movement, as shown by the clinical thermometer, as a general improvement in the feelings of the patient, attended with a slight depression in the temperature, a more marked diminution in the force and rapidity of the pulse, and a still more marked alleviation of the nervous symptoms, headache, restlessness, etc. The type of the disease is determined by the time of recurrence of these periodic remissions. The quotidian type is by far the most common; the tertian is not infrequent, but the quartan is extremely rare.

Next, perhaps, to the quotidian is the double tertian, having a daily paroxysm, but that of one day differing from that of the next, and the alternate paroxysms resembling each other both in character and in time of occurrence. Thus the paroxysm may occur one day in the morning, and the next in the evening; and all the morning paroxysms shall be in some manner modified, either very light and short, or without chill or perspiration, or attended with nausea, while those of the evening are attended with headache. A remittent may be considered of the double tertian type, when, having an exacerbation every day, it is yet much worse on alternate days. Sometimes two exacerbations occur in one day, and only one in the next; and cases are met with in which the principle of association between the exacerbations cannot be traced, as

> they every now and then make their appearance irregularly and when least expected (Wood [1]).

We believe that in simple malarial remittent fever, where no complication exists, a remission may always be detected by close observation within a period of forty-eight hours. Most medical writers, however, and especially those whose observations have been made in the tropics, admit that malarial remittent fever may assume a "continued form"—we prefer to say continuous—and Professor Wood says that "instances do occur, though they are comparatively rare and always short, in which the fever pursues a uniform course without discoverable relaxation, and sometimes with a regular increase, to the crisis."

The *time of day* at which the initial chill inaugurating an attack of remittent fever is likely to occur is by no means uniform. Wood says that the first onset of the disease seems to take place indifferently at any hour of the day, and occasionally even at night. Dr. O. F. Manson, who has had an extended experience in the vicinity of Richmond, Va., says that according to his observation the initial chill *never* occurs during the night "between the hours of 9 P.M. and the rising of the sun the following day," but that it commonly occurs in the morning "between the hours of 8 A.M. and 12 M."

DURATION.—The duration of remittent fever is doubtless greatly influenced by treatment, and opportunities for studying the natural history of the disease are rare. Still we have estimates relating to the duration of the disease which have a certain value. Professor Wood says:

> If the disease retains a distinct paroxysmal character it generally runs on, when not interrupted, for two or three weeks or more, terminating at last either by spontaneous solution at the end of one of the paroxysms, which goes off usually with a more than ordinarily profuse perspiration, or in a regular intermittent, or in a kind of low typhoid affection.

On another page the same author remarks:

> The average duration of bilious fever, in all its forms, may be stated at about fourteen or fifteen days. It sometimes ends as early as the fifth or seventh, often about the ninth or eleventh, and is sometimes greatly protracted, even to four weeks or more.[2]

Maclean fixes the duration at from five to fourteen days. Fayrer says that in favorable cases amendment begins in from six to eight days, or sooner. And according to Maury:

> In early summer with appropriate treatment this fever often terminates on the third day; as a rule it subsides on the fifth day. In the fall it is occasionally prolonged until the seventh, and in a very few instances I have seen it prolonged to the ninth day. Even without medical treatment it shows a marked tendency to defervescence on the fifth day, and will often do so completely without the aid of quinia, under the influence of rest, liquid diet, and cold-water treatment.[3]

The author last quoted is of the opinion that Dr. Wood's description of remittent fever includes two entirely distinct forms of disease, one of which is of short duration, and may with perfect propriety be styled bilious remittent or malarial remittent.

> In its course and duration it is as well defined, and as distinctly limited as acute pneumonia or any other form of fever with which we are acquainted. The record of these

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[1] Op. cit., vol. i., p. 278.

[2] Op. cit., vol. i., p. 286.

[3] A Clinical Contribution to the Study of Fevers of the Mississippi Valley. By Richard B. Maury, M.D., of Memphis, Tenn. Am. J. M. Sc., Phila., April, 1881.

forms is one which may, with equal propriety, be called malarial continued. It also runs a definite course. . . . It is self-limited, and cannot be jugulated or shortened by any known means."[1]

We would remark with regard to these protracted cases "which cannot be jugulated or shortened by any known means," that it is difficult to believe that they have the same etiology as the cases which yield promptly to the administration of quinine.

Dr. Manson says, in giving the history of "mild remittent fever," that it usually terminates, without the interference of art, in one of three modes, viz.: first, in grave remittent; second, in adynamic remittent; third, in intermittent.

When the disease terminates in recovery, as it usually does, the fever generally culminates in a profuse perspiration, and so ends. In other cases the amendment is gradual, the exacerbations become less severe, and the remissions longer, and in this way the fever gradually subsides. Again, the termination is not infrequently, in intermittent, of a more or less protracted character (Maclean).

Hertz says that the *first grade* of remittent fever usually terminates in recovery in three, five, or ten days; while, according to Griesinger, the *severer forms* last from seven to fourteen days.

SYMPTOMS.—After the premonitory symptoms heretofore mentioned—epigastric distress, malaise, pain in the head, back, etc.—or without any premonition, an attack of simple remittent fever is commonly inaugurated by a chill of brief duration. This sometimes amounts to a distinct rigor, but is seldom so severe or protracted as in intermittent fever, and often consists simply in a slight chilly sensation, or alternating flashes of heat and cold. The temperature is shown by the thermometer to be already somewhat elevated while the patient experiences the sensation of cold, and the body heat may be several degrees above the normal while the extremities feel cold to the touch; chilly sensations sometimes continue for some time after reaction has taken place, from the slightest exposure of the body, or even from contact with the hand of the medical attendant. The pulse is small, more or less irregular, and usually not much increased in frequency during the cold stage. The breathing is somewhat irregular and sighing; the patient is restless, and is often distressed by nausea, frontal headache, and lumbar pains.

As febrile reaction becomes established the pulse gains in force and frequency, the skin becomes hot and dry, the face is flushed, and the conjunctivæ injected. Headache is now often a very distressing symptom; it is described as throbbing or rending, and is aggravated by the frequent attempts to vomit. This, together with the pains in the loins and limbs, and burning heat, causes so much suffering that the patient tosses about in bed in the vain attempt to obtain an easy position. In sthenic cases, and especially in those occurring during the hottest season of the year, these symptoms are particularly severe; the headache becomes intolerable; the pulse is full and bounding, and 100 to 120 per minute; the vomiting or attempts to vomit incessant, and the temperature may quickly mount to 107°, or even more than this. Delirium is not infrequent during the febrile exacerbation in these cases. If these symptoms continue without any decided remission for several days, the case is of the variety described by some writers as "inflammatory remittent," and which we shall describe under the heading "Ardent Malarial Fever." In simple remittent all of these distressing symptoms disappear, or at least are greatly moderated during the remission.

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[1] Ibid., p. 396.

Many cases are inaugurated in a much milder fashion than this, and with the exception of slight headache, lassitude, some gastric oppression, and ill-defined pains in the back and limbs, the patient has nothing to complain of. In asthenic subjects the pulse is frequent but compressible, and the febrile reaction is not so intense.

The tongue is at the outset more or less heavily covered with a white, or bluish-white, coating; the margins are red and often indented by the teeth, or present the appearance which Dr. Osborn has described, and which we have referred to in detail in the article on "Malarial Intermittent Fever" (page 148).

The secretions of the mouth are viscid and tenacious, and a glairy mucus often accumulates in the fauces, which gives rise to frequent hawking and spitting. In "Chagres fever" the attack is said to be often ushered in by catarrhal symptoms (Buel).

The Remission.—The febrile reaction, and the distressing symptoms which attend it. usually reach their acme of intensity in from six to twelve hours. After this the remission occurs. This is characterized by an abatement of, or more commonly a complete relief from, the headache, vomiting, and thirst; by a reduction in the temperature, and in the force and rapidity of the pulse; and by the occurrence of a gentle perspiration —sometimes copious—which appears first upon the face and neck and gradually spreads over the whole body. Usually a daily remission occurs, and in mild cases this may last for several hours, commencing late in the afternoon—usually between the hours of five and eight in *very mild* cases (Manson)—and continuing until the following morning; in more severe cases the remission is less complete and of short duration, and close observation is often necessary in order to detect it. The pulse will often give the only indication (Maclean). In cases of the tertian type the remission may last a whole day. The patient often obtains some sleep during this period, and may take a little food. The remission in a large majority of the cases occurs during the early morning hours, or if it occurs during the night lasts until morning.

> It is a point of great practical importance to observe in each case the periods of exacerbation and remission, and the duration of each. If the exacerbation begins at noon, it will usually decline about midnight, or a little before, and the remission will last till noon the next day. Such cases are usually comparatively slight and manageable. Or the exacerbation may begin at midnight, continue all night, and remit in the morning, the remission lasting till midnight. Or, in severe cases, there may be a double exacerbation, at noon and at midnight, the remissions being in the evening and morning, the last being invariably the most distinct. When the disease assumes this type, the evening remission is sometimes so slight as to escape notice; but for the invariable morning remission it might be mistaken for a continued fever (Maclean).[1]

In many cases the exacerbation is more violent every second day, and these cases have been supposed by most writers to be of the double-tertian type. But if the remission occurs at the same hour each day, we should agree with Manson in calling the type quotidian; this, however, is not a matter of any practical importance. In some cases each succeeding exacerbation is inaugurated by a chill; but as a rule the patient does not experience the sensation of cold, although his extremities may be below the normal temperature, and the lips and fingers may have, for a brief time, the livid appearance seen in the cold stage of an intermittent. With or without this brief cold stage the succeeding exacerbations pursue the same course as the first; the headache and bilious vomiting return, and the pulse regains its former force and frequency. In a majority of the cases there is more or less tenderness, on pressure, in the epigastrium, which is sometimes excessive, "so that the patient cannot bear with equanimity the touch of the fingers." This epigastric tenderness is generally not experienced in any considerable degree before the third or fourth day (Wood). Complaint is sometimes made of a severe burning pain in the region of the stomach.

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[1] Article in Reynolds' System of Medicine, vol. i., p. 70.

Nausea and vomiting often occur at the outset, and in severe cases become more distressing as the disease progresses. The matter ejected is sometimes nothing more than a little glairy mucus and the fluids swallowed, but more commonly it is bilious in character, of a yellowish or greenish hue, and of an acrid or intensely bitter taste. Mild cases may run their course without any gastric disturbance, and the cases in which this is excessive belong rather to the category of "gastric remittents" than to that of "simple remittent fever." The bowels are commonly constipated at first; but copious bilious discharges are usually induced by cathartic medicines. Sometimes large watery evacuations appear early in the disease, at other times when it is passing away (Maclean).

The *urine* is scanty and high-colored during the febrile exacerbation, but more copious, of lower specific gravity, and of lighter color during the remission. It is invariably acid, and commonly deposits a lateritious sediment on cooling. In this form of remittent fever it is free from albumen.

Delirium is not frequent in simple remittent fever, except in the case of children and of aged persons, during the height of the febrile exacerbation. Sometimes, however, delirium occurs of a violent character, forming, apparently, an alarming and dangerous feature. Even in these cases, however, it almost invariably disappears before the next paroxysm (Manson). Delirium which does not disappear during the remission is an indication of a cerebral complication of an inflammatory nature.

Convulsions, usually of brief duration, may occur in young children during the febrile access. According to Manson they are rarely a source of danger when they occur in the early part of an attack.

The *spleen* is often considerably enlarged, but this is commonly the result of antecedent attacks of intermittent. Probably because of the comparatively brief duration of the disease, and the short cold stage, the spleen is less subject to enlargement than in intermittent fever. Some degree of enlargement may commonly be detected, however, upon a careful examination.

Some degree of *yellowness of the skin* is said by Wood to be a common feature of remittent fever. This is true as regards the bilious form of the disease, but it is far from being a constant symptom, and many cases of simple remittent occur which cannot properly be called "bilious fever," a term which is frequently used as synonymous with "remittent fever."

Professor Wood says: "One of the most striking characteristics of the disease, though not present in all cases, is a yellowish hue of the skin and of the white of the eyes. This sometimes makes its appearance at the beginning, but more frequently not until about the third or fifth day of the disease. It is often uniform over the whole body, and before the close is very intense. In some bad cases it assumes a dark or bronzed hue. Occasionally the yellow matter is thrown off upon the surface so as to stain yellow a white handkerchief rubbed upon the skin."[1]

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[1] Op. cit., vol. i., p. 281.

A slight icteric tint, developed after several days of sickness, is no doubt a common feature of the bilious form of remittent fever, but the intense jaundice referred to is rather a complication than a symptom of ordinary remittent.

> Colin says: "In a certain number of cases attacked with the symptoms of the preceding form" (gastric form) "we see developed, at the decline of the fever, a yellowish color, which invades little by little the cutaneous surface as the capillary congestion disappears; the sclerotic is the most evident seat of this; it sometimes happens that this transformation of color occurs suddenly, and it is a surprising thing to find a patient icteric and without fever, that we have left the preceding evening with fever and covered with a suffusion almost scarlatiniform. This phenomenon recalls that which manifests itself in yellow fever, at the termination of the first stage of the disease, which has been attributed to a coloration of the skin by the pigmentary material of the blood."

This may be the true explanation of the suddenly developed icteric coloration in certain severe cases. More commonly, however, the discoloration is due to bile-pigments.

The *bilious form* of remittent fever, according to Colin, occurs more frequently late in the season, and among those who have previously suffered attacks of malarial fever. Thus the proportion of cases of this form in his wards, in Rome, during the month of July, 1864, was about one to twenty, compared with the "gastric form," while during the last week in August it was as one to four. The few cases in September were nearly all of the "bilious form." This name is reserved by Colin for those cases in which there is abundant bilious vomiting and free intestinal evacuations of the same character, and in which the icteric suffusion is primitive. It would seem from this that malaria is a larger element in the etiology of this form, which occurs during the season of intermittents and in malarial subjects—"*les anciens fébricants*"—than in the "gastric form," in which heat is evidently a prominent and essential factor, although insufficient by itself to account for the annual endemo-epidemic, which occurred with such regularity among the French troops in Rome, and in which a vast majority of the cases were of this form—denominated "gastric" by Colin, and corresponding with the "*forme inflammatoire*" of other French authors. We shall consider this form of fever separately, as it does not seem to us to come properly under the heading "simple malarial remittent fever."

DIAGNOSIS.—The diagnosis of simple remittent fever presents no difficulties. It occurs in persons who have been exposed to malarial influences; is characterized by distinct remissions, which usually occur in the morning; and may be aborted or cut short after several days, by the administration of quinine. This form of remittent fever does not prevail as an epidemic, and it is a disease of the country rather than of the city. Those who fall sick with it in non-malarious localities present the history of former, and usually recent, exposure. After a visit to the country, or after crossing the Isthmus of Panama, or after a hunting expedition, a denizen of one of our large cities may fall sick with malarial remittent fever. Those who reside permanently in malarious localities are at all times subject to the disease, and it may recur in the same individual an indefinite number of times. When we hear that "remittent fever" is prevailing as a fatal *epidemic* in a certain seaboard or interior *city*, it is entirely safe to say that it is not this form of remittent fever, although we may not have seen any of the cases.

It must be remembered that the remission may be very well defined and characteristic, without any very marked reduction occurring in the body heat, as shown by the clinical thermometer. The headache and nausea disappear, the extremities become cold, a gentle moisture bedews the surface, and the pulse is greatly reduced in force and frequency, but to our surprise the thermometer only shows a reduction of one or two degrees in the temperature. This applies to the more severe cases ; when the disease is of a milder character the temperature often falls nearly to the normal, and, as we have previously remarked, the case may be so nearly on the borderline that it is a matter of doubt whether to call it remittent or intermittent. Professor Manson, of Richmond, Va., whose practice has been in a region where remittent fevers of undoubted malarial origin are very prevalent, gives the following account of the "pathognomonic chill of remittent fever :"

> This, according to my observations, *never* occurs between the hours of 9 P.M. and the rising of the sun of the following day, but usually between the hours of 8 A.M. and 12 M., and occasionally between 6 and 8 P.M.
>
> At or near these periods, the watchful attendant will perceive a sensible diminution of temperature of the extreme parts, viz., the nose, toes and fingers, or the whole hands and feet will be found below the natural standard, being cool and damp, *the rest of the surface retaining its febrile heat*, more evident in the cerebro-spinal and epigastric regions. In this condition the patient rarely complains of any sensation of cold, but often of heat, desires to be fanned, the clothing to be removed, and entreats for cold drinks. The pulse is frequent, but usually regular ; the bowels torpid but easily excited into action. Nausea and vomiting are sometimes present, the fluids ejected from the stomach being usually of a bilious character. The respiration is not much affected, but the patient yawns and gapes, utters deep sighs, alternating with forcible voluntary expirations. The duration of this stage is usually brief, rarely lasting more than an hour, and is succeeded by the reaction, which is marked by an extension of the febrile heat over the whole surface, etc.[1]

The differential diagnosis between this form of malarial fever and yellow fever may be established as soon as well-defined remissions are detected ; for in the latter disease the febrile movement has quite a different character. The acme of pyrexia is very quickly reached, and from this point the course of the temperature curve is downward, for a period of from three to eight days, during which it constantly approaches the normal or falls below it. It is true that slight elevations sometimes occur to interrupt the uniformity of this downward tendency, and that the "stage of calm" in severe cases is followed by a reactionary fever, which has a remittent character. But the continuous character of the initial fever, the profound depression of the vital powers during the apyretic period, the presence of albumen in the urine, and the fact that when vomiting occurs it is not of a bilious character, will make it a simple matter to establish a differential diagnosis between this pestilential disease and simple malarial remittent fever. Moreover, the latter, as we have already remarked, is a disease of the country, and especially of marshy localities, and does not prevail as an epidemic ; whereas yellow fever is a disease of towns and cities, and especially of seaport towns, and the cases at the outset of an epidemic are grouped around certain infected centres, or traceable to infected ships. The differential diagnosis from mild cases of typhoid fever is not so easy at the outset, and in many instances is, perhaps, quite impossible. But as the case progresses it is established by the fact that the latter disease is not favorably influenced by the administration of quinine and runs a protracted course ; whereas simple malarial remittent fever is very amenable to specific treatment, especially those mild cases which are most apt to be mistaken for commencing typhoid. In severe cases the abruptness of the onset, the distressing headache and gastric disturbance, and the characteristic remission, together with a history of exposure to malarial influences, enables one to exclude enteric fever very promptly. In the milder cases a detection of the "pathognomonic chill of remittent fever" described by Dr. Manson will no doubt frequently aid in establishing an early diagnosis.

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[1] Va. Med. Monthly, Oct., 1881, p. 504.

Prognosis.—Under proper treatment the mortality from simple remittent fever is practically *nil.* This arises from the fact that we have separated the graver forms of the same disease, which frequently do kill, under the headings "Pernicious Remittent Fever" and "Adynamic Remittent Fever." This distinction is quite an artificial one, but so is the distinction between intermittent and simple malarial remittent fevers, and for purposes of clinical description one line of division is quite as justifiable as the other. Even where all cases of "remittent fever," not congestive, are included under one heading, as in our army statistics, the reported mortality is small (see page 90). This results from the fact that the graver and fatal varieties are less common in this country than the simple remittent which we have just described, which accordingly is the leading form in determining the mortality rate. But in tropical countries other and more fatal forms take the lead, and the mortality from fevers called "remittent," is in some parts of the world enormous. Maclean says:

> Death from an uncomplicated remittent fever ought to be a rare occurrence, and, under good management, so it is. Even in ardent cases in sthenic constitutions the prognosis is favorable; and, if skilfully treated, recovery may be confidently looked for in a large majority even of advnamic cases, if seen sufficiently early.

Fayrer says:

> The character of the remissions, and the early or deferred return of the exacerbations, are indications of the probable severity or lenity of the attack. Well-marked remissions, free diaphoresis, diminished temperature, and headache or cerebral symptoms are favorable indications; whereas higher fever, ill-defined remissions, accelerated exacerbations, with delirium, coma, and typhoid symptoms, vomiting of blood and bile or symptoms of collapse as the hot stage is passing away, indicate great danger. . . . In favorable cases amendment begins in from six to eight days or sooner; the remissions become more complete; the patient sweats freely; the tongue begins to clear and moisten at the edges, and the sordes disappear; the headache and thirst diminish, and the appetite begins to return; he perhaps sleeps and then gradually regains his strength. Such is the state of things in a simple attack of remittent, and the prognosis is generally favorable; but the brain, the lungs, or the abdominal viscera may become implicated, causing serious complications.[1]

Treatment.—The treatment of simple remittent fever is practically the same as that recommended for intermittent. The object in view is to arrest the course of the fever as promptly as possible by specific medication; and for this purpose the salts of quinine are to be preferred to the other cinchona alkaloids or to any medicines whatsoever. The evidence in favor of the superiority of quinine—the sulphate, disulphate, or muriate—is so convincing that the substitution of other remedies on the score of economy, or for any other reason, does not seem justifiable when this can be obtained.

Formerly the opinion prevailed that a certain course of preparatory treatment was necessary in order that quinine might favorably influence the course of the fever. This idea no longer controls the practice of intelligent physicians in malarious regions. It is true that quinine is useless if, owing to a hyperæmic condition of the gastro-intestinal mucous membrane, it is not absorbed, or if from gastric irritability it is immediately rejected; and inasmuch as its effects are not immediate, and as it sometimes adds to the headache and gastric disturbance when administered during the height of the febrile exacerbation, most practitioners prefer to give during the remission the full amount which they think may be required to control the course of the fever. This is well enough in the mild cases in which there is a well-marked remission; but when there is no doubt as to the malarial character of the disease, it is worse than useless to delay more than a few hours, or to allow an imperfect remission to pass without resorting to specific medication. Gastric irritability may contraindicate the administration of quinia by the stomach, but we have left the resource of giving it by enema or by hypodermic injection. The quantity to be given will depend upon the severity of the malarial intoxication, and the object in view should be to produce the physiological effects of the drug as promptly as possible.

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[1] Op. cit., p. 95.

As a general rule we should say that in ordinary remittent fever from twenty to thirty grains, given during the period of least febrile excitement, will be the proper amount to give to an adult during each twenty-four hours, for the first three or four days of the attack. A very good plan is to give the required amount in two doses, one to be given at bedtime—eight to ten o'clock—and the other during the morning remission. Fayrer says:

> I have ceased to regard pyrexia as an obstacle to the administration of quinine, for though this is more effective when given during the remission, I have often seen it of service in adynamic conditions of remittent when given in all the stages; and I have so often seen it reduce temperature in other febrile states that I never hesitate to give it during the pyrexia of malarial remittent.[1]

Maclean says, with reference to the administration of quinine during the exacerbation:

> In the adynamic form of the disease, such as I described as coming from the malarial quarters of the city of Hyderabad, I never waited for a remission, but gave it at once by mouth or rectum, or both. . . . The American physicians led the way in this practice and demonstrated its safety.[2]

The unfounded prejudice against giving quinine during the febrile stage of a remittent fever has to a great extent given way, since experience has demonstrated that in a full dose it is a most potent antipyretic remedy, and there is no contraindication to its use at this time except that referred to, viz., the possibility of its being rejected by the stomach. We are inclined to think that a full sedative dose—thirty grains—administered at any time during the stage of febrile excitement, will be found more effectual in reducing the temperature than diaphoretics, more useful in calming nervous excitement than opium, and the best remedy for the relief of headache. But not having had an opportunity to test the value of such sedative doses during the pyretic stage of simple remittent fever, since we have learned to use the medicine in this manner for the relief of excessive pyrexia in enteric fever, we simply make the suggestion without feeling authorized to recommend a departure from the usual custom of giving quinine in divided doses during the remission.

If a cathartic is indicated, ten grains of calomel, or the same quantity of blue mass, may be given with the evening dose of quinine. We prefer to administer the medicine to adults in the form of *freshly made pills*—very moderately sized pills, containing three grains each, may be made by the use of tartaric acid and glycerine in making the pill mass. Those who object to taking pills may take the quinine in capsules, or suspended in water, or in milk. The combination of calomel or blue mass with quinine—*e.g.*, ten grains of each—has seemed to us more efficient as a cathartic than is the mercurial when administered alone. Very commonly the bowels are freely moved on the following morning. If this is not the case a seidlitz powder, a glass of Hunyadi Janos, or a bottle of effervescing citrate of magnesia may be given. A cathartic is nearly always indicated at the outset, and the preference with most practitioners in malarious regions is for a mercurial. Many prefer to combine with this some medicine which insures its cathartic action. Dr. Manson gives habitually ten grains of calomel and ten of rhubarb. Maclean says: "It is well also that the bowels should be thoroughly cleared as soon as possible. For this purpose, from three to five grains of calomel, extract of colocynth, and scammony should be given, with a few drops of any aromatic oil. I have found this combination very effectual; it rarely, if ever, gripes or causes nausea; it appears to act on the whole tract of the intestine, and seldom requires a nauseous draught to aid its operation." The compound cathartic pills of the U. S. Pharmacopœia, are, perhaps, quite equal to the combination recommended by Professor Maclean, and are extensively prescribed in this country. They also may be given with the evening dose of quinine.

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[1] Op. cit., p. 110.

[2] Op. cit., p. 79.

Hypercatharsis is to be avoided, and a frequent repetition of the purgative medicine, recommended as commonly useful at the outset of an attack, can only do harm. The coated tongue clears up, and the gastro-intestinal irritation is relieved when the patient is brought fully under the influence of quinine, but no amount of purging will accomplish the same result; whereas drastic cathartics may induce inflammation, where before there was simply hyperæmia due to vaso-motor paralysis. Morehead gives the following sound advice with reference to the administration of cathartics:

> During the first two or three days of the attack, when the tongue was foul but not florid, the alvine excretions vitiated, the abdomen full and resisting, and the vascular excitement steady and without tendency to depression, it was an important part of the treatment to give a ten-grain dose of calomel, combined with a few grains of antimonial powder, and some hours afterward an aperient, as the compound powder of jalap. The calomel was generally administered at bedtime, and the compound powder of jalap in the morning. Calomel and purgatives, even to the extent now recommended, are seldom expedient after the third or fourth day of the disease, and they are unnecessary, even at an earlier period, if the abdomen be soft and without fulness, notwithstanding the presence of disordered alvine excretions and a coated tongue.[1]

On another page this distinguished clinical teacher protests against the practice of giving repeated doses of calomel during the continuance of the fever. He says:

> The practice, at one time too common, of exhibiting calomel in doses of four or five grains three or four times in the course of the day, without any very definite object, and continuing it for a succession of days, cannot be too strongly condemned. Not only is it unnecessary, but, for the following reasons, positively injurious: 1. In watching the progress of cases thus treated it is not difficult to detect a train of symp-

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[1] Op. cit., p. 110.

> toms more fairly attributable to the treatment than to the disease, because it is in cases thus treated that it has been chiefly observed. The symptoms alluded to are uneasy feelings, sometimes amounting to pain, with a sense of oppression or sinking at the epigastrium, and occasional griping of the abdomen, for which leeches are not unfrequently applied and purgatives given. 2. The frequent repetition of the calomel keeps up a furred state of the tongue, with nausea and irritability of stomach, aggravates the febrile excitement, and produces an irritable state of the bowels, indicated by frequent watery discharges. 3. The convalescence of cases thus treated is always tedious, and frequently complicated with diarrhœa and clay-colored dejections. . . .
>
> Not only is the practice unsound in theory and of no value, but it is contrary to all rational theory, and very injurious. If it be true that prostration of vital actions and a deteriorated state of the blood are very unfavorable conditions in remittent fever, and that mercury deteriorates the blood and favors prostration, on what principle of reasoning can it be maintained that mercurial influence induced by the physician can have any other than an injurious effect in remittent fever? I have on several occasions pointed out the tendency of malarious fever to produce a cachectic state of the system, and have endeavored to inculcate the importance of guarding against the increase of this unfavorable diathesis by medical treatment. To all who within the last twenty years have had an opportunity of extensively observing disease in India, in the various classes of the European community—asthenia, dyspepsia, injured teeth, pains of sides and loins, palpitation, habitually foul tongue, constipated bowels, pale alvine evacuations, depressed spirits, and a sense of sinking at the epigastrium—all traceable to the abuse of mercury—must be familiar facts. Such then are the reasons, drawn from my own sphere of observations, which have led me to the conclusion that the induction of mercurial influence in the treatment of malarious fever has been a great and grievous error in therapeutics.[1]

It is to be feared that this "grievous error in therapeutics" has not been entirely corrected in our own country, notwithstanding the fact that Dr. J. Forsyth Meigs showed us more than fifteen years ago, by the favorable results obtained in the treatment of one hundred and seventy-six cases of malarial fever—intermittent and remittent—in the Pennsylvania Hospital, that it may be dispensed with entirely in these cases. In the valuable paper from which we have already quoted extensively with reference to changes in the blood, etc., Dr. Meigs at the close of his remarks upon treatment refers to the use of mercury in the following language:

> Mercury was scarcely employed at all. A few blue pills were given when the bowels were rigid and the skin very sallow, but certainly not more than twenty blue pills were used in all the cases, and calomel was proscribed as unnecessary, and likely to be injurious by its debilitating effect.
>
> No drastic cathartics were allowed. Rhubarb in moderate doses, a Seidlitz powder, or small doses of Rochelle salts were resorted to when the bowels were decidedly torpid, but, if the patient had a spontaneous evacuation every day or two the bowels were left undisturbed.
>
> I desire to call particular attention to the very small amount of mercury used in these cases. I believe that the old American system of giving calomel and jalap, or calomel in ten or twenty grain doses, as a cathartic, or in one or two grain doses, every two or three hours, as a cholagogue or alterative, is positively dangerous from the debility which they cause, and from the gastric and intestinal irritation which they sometimes set up. To say the least they are unnecessary, and any one who has seen the gastric distress, intestinal irritation, or the constitutional poisoning which mercury not infrequently induces, will be glad to know that he may, with a good conscience, dispense with its use in so severe and dangerous a disease as this of malarial fever often is. To know that one hundred and seventy-six cases of malarial disease, many of them very severe in their type, were treated almost without mercury, with only six deaths, is surely proof enough that this drug is not essential. And when it is recollected that of the six deaths one occurred in an hour and a half, and another in twenty hours after admission, one of dysentery after recovery from the fever, and one of acute tuberculosis, leaving only two deaths in one hundred and seventy-two cases fairly ascribable to the malarial disease after proper treatment, it must be plain that mercury, except in very small doses, may be safely dispensed with.[2]

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[1] Op. cit., p. 127.

[2] Op. cit., p. 125.

An emetic is sometimes useful at the outset of an attack when there is nausea without vomiting, and no epigastric tenderness. The stomach may be washed out by draughts of tepid water, to which a scruple of powdered ipecac, or a teaspoonful of mustard may be added, if necessary, to produce an emetic effect. Gastric irritability is to be combated by the use of sinapisms, or of chloroform—on a handkerchief or piece of lint—applied to the epigastrium; by swallowing small bits of ice; or by the use of cold effervescing drinks, such as iced soda-water or citrate of potash.

During the febrile exacerbation diaphoretics may be prescribed to advantage, and one of the best of these is, perhaps, the effervescing citrate of potash, so highly recommended by Professor Wood. This author says of his favorite remedy:

> It is one of the most efficacious means of correcting nausea and vomiting, and acts more certainly and powerfully as a diaphoretic than almost any other saline substance with which I am acquainted; tartar emetic itself scarcely constituting an exception. It sometimes occasions griping pains in the stomach and bowels, with frequent small evacuations; but this tendency may be corrected by the addition of four or five drops of laudanum, or about twenty drops of the officinal solution of sulphate of morphia to every other dose.

Minute doses of the tincture of aconite root, frequently repeated, often have a favorable effect in moderating the intensity of the febrile movement. One-half drop to a drop, combined with fifteen drops of spiritus ætheris nitrosi, may be given every hour during the exacerbation, if it be decided to wait for a remission before resorting to specific medication. No doubt a "Dover's powder" at bedtime is often useful in producing diaphoresis and quieting nervous excitement. According to Dr. Wood this medicine given in doses of ten grains every six or eight hours is more suited to asthenic cases and to advanced stages of the disease. "When there is headache, with great heat and dryness of the skin, and a full and frequent pulse, morphia is contraindicated" (Morehead). But in the absence of these conditions a full dose of opium or morphia may often be given at bedtime with advantage. As a general rule, however, we believe that very little symptomatic medication will be required in simple remittent fever, and that the external application of cold water for the relief of headache, the sponging of the surface of the body with tepid or cold water for the reduction of temperature, and the swallowing of bits of ice to relieve nausea, may constitute the entire treatment of the pyretic stage in mild cases. And in the graver cases we think with Maclean that "practitioners who relax in their efforts to stop the exacerbations, who pause in the use of quinine while they apply routine remedies for this or that symptom, now applying leeches to the head because delirium or headache is present, to the epigastrium because there is some tenderness there, will have little success in the treatment of the worst forms of Indian remittents," or of malarial remittent fevers in any part of the world.

The specific medication must be continued until the progress of the disease is arrested, and then smaller doses of quinine will be required for several days to prevent a relapse. Six grains morning and evening will be a proper dose for this purpose, and after three or four days, if all goes well, one-half this quantity will probably be sufficient to assure a steady convalescence.

That simple remittent fever may commonly be arrested within a brief period by specific medication of the kind indicated is proved by the testimony of numerous physicians; and when quinine proves impotent to control the course of the disease, it is no doubt, in the great majority of cases, due to some complication, or to the fact that the remedy has not been absorbed, or to its having been given in insufficient quantity, or to a mistake in diagnosis.

Professor Manson says: "Under this simple plan of treatment, remittent fever, as it appears usually in this section" (Richmond, Va.), "is certainly and safely cured. *We have in this manner arrested the disease in many hundred cases, in one night.*" It is but fair to state, however, that the simple treatment referred to includes the application of leeches to the temples, and leeches or cups to the epigastrium, for the relief of headache and gastric disturbance. We take the liberty, however, of assuming that this local depletion, or the moderate bleeding from the arm, which is said to be "rarely necessary," is an unessential part of the treatment, so far as the cure is concerned, although no doubt effectual for the relief of the symptoms to which it was addressed. Dr. Manson's practice is to commence the treatment with a cathartic dose of calomel and rhubarb, 10 to 12 grains of each, at bedtime; and to give 10 to 20 grains of quinine "at some period before or after midnight, when the fever will generally be found more or less to decline." This is followed, at intervals of three or four hours, by doses of 5 or 6 grains until the period of chill has passed, "generally exhibiting from 25 to 40 grains before that time."

The prompt relief which may often be obtained in mild cases is shown by the following extract from a letter to the *Boston Medical and Surgical Journal*, written by Dr. George Derby, Surgeon U. S. Volunteers, and dated Newbern, N. C., September 10, 1863:

> Remittent fever, which now prevails in the regiments about here, is controlled by quinine in a manner truly surprising. A man is found with hot skin, very frequent pulse, headache, nausea, tender epigastrium, anxious expression. Give him ten to twenty grains, and in a large number of cases you find him on the next visit, or twelve hours afterward, with convalescence established.

The power of quinine to abort an attack during the formative stage, in a comparatively severe form of the disease, the so-called "Chagres" or "Panama fever," is shown by the following quotation from a paper, already referred to, by Dr. William P. Buel, Surgeon of the Pacific Mail Company (1856). The evidence given by Dr. Buel is especially interesting, as the form of fever referred to is undoubtedly malarial, and during the time of his service large numbers of persons on their way from Atlantic seaports to San Francisco contracted this fever during the brief period occupied in crossing the isthmus.

> An incubation period of several days, usually not less than a week, elapses between the time of exposure and development. On board steamers leaving Panama for San Francisco, this is about the time usually occupied in arriving at Acapulco. Cases of fever begin to occur in considerable numbers within two or three days after leaving that port. The patient experiences, for two or three days before the attack, a general soreness and tenderness in all the muscles and integuments, with loss of appetite and debility, but does not consider himself seriously ill. He is next attacked with severe frontal headache, pains in the lumbar region, in the epigastrium, and in the extremities. There is usually more or less of catarrhal symptoms, coryza, sternutation, etc. He thinks it probable he has taken cold from sleeping on deck a night or two previous. The first attack is not usually ushered in by a regular ague, though the patient often complains of feeling chilly. He has a peculiar anxious expression of countenance, and a contracted brow, which to a familiar observer are almost diagnostic of the disease. . . . In this formative stage of the disease, without resorting to any preliminary treatment whatever, the prompt administration of ten or fifteen grains of quinine in a

> single dose is followed by almost immediate relief. The severity of the headache and other nervous pains is at once alleviated. The countenance of the patient loses its anxious expression, the contracted brow becomes dilated, and his whole aspect indicates that a favorable change has occurred. The repetition of the quinine, at intervals of twelve to twenty-four hours, two or three times, is followed, in almost all cases, by the disappearance of all the symptoms and a complete restoration to health, with the exception of some remaining debility. If the practitioner, ignorant of the disease he has to treat, or guided by preconceived notions or prejudices, should commence the treatment by administering emetics, or large doses of mercurial cathartics, instead of any great relief of the symptoms he will find them all greatly aggravated.[1]

The *bilious form,* which we have included under the heading "Simple Remittent Fever," does not commonly yield to treatment so promptly as do those typical mild cases which are unattended with bilious vomiting or marked gastric disturbance. But in this form, also, quinine is the sovereign remedy, and when the patient is fairly brought under its influence the bilious vomiting and other distressing symptoms will often disappear as if by magic. On the other hand, persistence in the use of emetics and mercurial cathartics "to get rid of the bile in the system," only increases gastric and intestinal irritation, and prolongs the duration of the attack. Perhaps the main reason why this form of the disease is less controllable by specific medication at the outset of the attack than even pernicious cases, unattended with gastric irritability, is because the medicine, commonly administered by the stomach, is not absorbed, even when not immediately rejected. Under these circumstances we have a valuable resource in the hypodermic method of administration, already referred to at length in the present volume (page 190). There is little danger of abscess if a solution made with tartaric acid is used, and the needle is made to enter the subcutaneous tissue, with the point turned away from the under surface of the skin. That is to say, if the patient was in a fair state of health prior to the attack of fever. In cachectic subjects the danger of abscess or sloughing is greater; and these accidents may occur no matter what solution is used, or how great the care taken in making the injection. In these cases, therefore, it is better to administer quinine—dissolved by means of tartaric acid or glycerine—by enema. Ten or fifteen drops of laudanum may be added to the enema with advantage. Thirty grains may be given in this way at the time of the physician's first visit, and we believe will be found more useful for the relief of headache and vomiting than any symptomatic treatment that can be adopted. It is especially important that the system be promptly brought under the influence of quinine in this form of the disease, for neglected or improperly treated cases often assume an adynamic type, and they are then much less susceptible to specific treatment.

Stimulants are injurious during the febrile exacerbation, even in asthenic individuals, and in sthenic cases are rarely admissible until convalescence is fairly established. They are contraindicated when there is much gastric irritability or pain on pressure over the epigastrium. In the absence of these symptoms they may be given during the remission to those habituated to their use. As a rule, they will not be required during the first three or four days of the attack. When, however, there is great depression of the vital powers during the remission they may be imperatively demanded; and in cases having an adynamic tendency they will often be required at regular intervals, and in considerable quantity, notwithstanding the fact that the temperature remains constantly several degrees above the normal.

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[1] Am. J. of the M. Sc., Phila., April, 1856.

Food.—In simple remittent fever not attended with gästric irritability, tea and toast, milk toast, soft-boiled or poached eggs, light farinaceous food of any kind, or a cup of coffee with bread and butter, may be permitted during the remission. But when the stomach is irritable liquid food only is admissible. Chicken-tea, beef-tea, and especially milk, should constitute the entire diet in these cases, until such time as the digestive function is fairly re-established. There is a prejudice against milk in many parts of the country, from a belief that "it is bilious." We believe this prejudice to be utterly without foundation, and that milk is the most valuable form of liquid food in this, as well as in other febrile complaints in which supporting treatment is indicated, and in which the stomach cannot bear solid food. It will not be required, however, during the first two or three days of an abrupt and violent attack, for the stomach is almost invariably irritable and the patient has not the slightest desire for food, which may be dispensed with entirely until the violence of the attack is somewhat moderated. Much harm is often done by forcing food—even liquid food of the simplest kind—upon a patient for the purpose of "keeping up his strength," when the stomach is not in a condition to absorb it, or is so irritable that it is sure to be rejected. Under these circumstances, to give the organ complete rest is better than medicine, and to tax its digestive power in any way is as unwarrantable as to ask a man with a sprained ankle to walk "just a little bit."

In sixteen well-marked cases of "ordinary remittent fever," treated in the European Hospital at Bombay, in accordance with the principles above laid down, the average period, from the commencement of the attack to the perfect cessation of all febrile symptoms, was six and one-half days; of these two were passed before admission, and four and a half under treatment in hospital." Dr. Morehead, to whom we are indebted for these facts, remarks:

> The time occupied in the cure is an important consideration from its bearing on the degree of efficiency of the patient after recovery; this will always be in proportion to the judgment displayed in abstaining from unnecessary depressants during the exacerbations, and in the early prevention of exacerbations by the adequate use of quinine in the remissions. The stage of convalescence, moreover, will vary according to the nature of the treatment and duration of the attack. If the management has been skilful, convalescence will be attended by little derangement of function, and will require only a moderate use of stimulants and special articles of diet; but if depletion, purgatives, and mercury have been used in excess, and quinine insufficiently in the remissions, convalescence will be characterized by much debility, splenic enlargement, dyspepsia, palpitation, intermittent headache, and tendency to diarrhœa or dysentery; and stimulants and extras will be largely consumed.[1]

Cases.—The following charts, Nos. 5, 6, 7, and 8, are from the paper by Dr. B. B. Maury, of Memphis, Tenn., to which reference has already been made (*Am. J. M. Sc.*, April, 1881):

Case I. *Quotidian Remittent* (Chart 5).—J. R. E——, aged twenty-one. Twenty grains of quinia given during each remission, beginning with the first. Defervescence on third day. Exacerbations occurred at 5 A.M. on first day, at 1 P.M. on second and third days.

At 6 P.M. on fourth and fifth days there was so severe an attack of intercostal neuralgia under the right breast, with inability to breathe in the recumbent position, as to necessitate hypodermic morphia. No elevation of temperature accompanied the neuralgic paroxysms. Quinia was given again on the fifth day.

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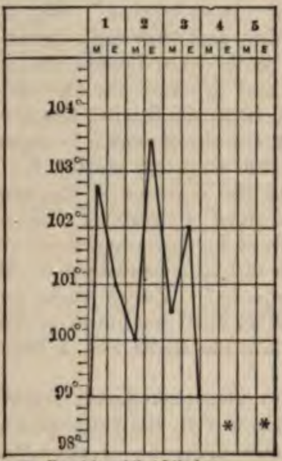
[1] Op. cit., p. 113.

CASE II. *Quotidian Remittent* (Chart 6).—J. R. E——, the same patient referred to in Case I. Taken sick three weeks after first attack. On fifth day the temperature rose higher that on any previous day of his illness, though quinia to the extent of twenty grains was given during each remission, beginning with the first. Defervescence occurred on fifth day. Exacerbations occurred at 4 A.M. on the first, 6 A.M. on the second and third, and 9 A.M. on the fourth and fifth days.

Quotidian Remittent Fever.



* *Neuralgia on 4th. & 5th. days.*

Chart No. 5 (Maury).

Quotidian Remittent Fever.

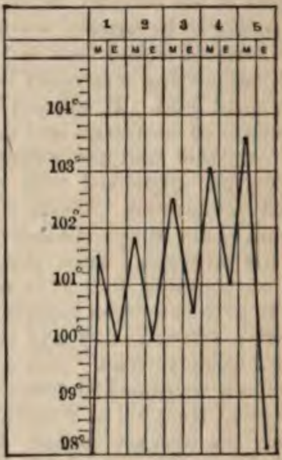


Chart No. 6 (Maury).

Quotidian Remittent Fever.

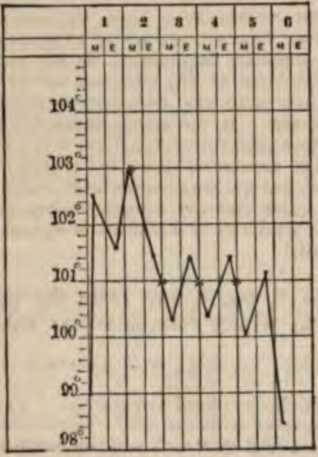


Chart No. 7 (Maury).

Double Tertian Remittent.

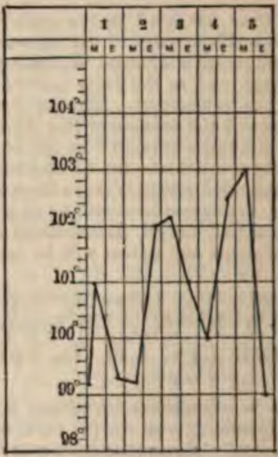


Chart No. 8 (Maury).

CASE III. *Quotidian Remittent* (Chart 7).—F. D——, a girl, aged fourteen. Quinia was given at the height of the second exacerbation, ten grains at 9, ten grains at 10, and ten grains at 11 A.M.—*i.e.*, thirty grains in two hours. Again between midnight and daylight twenty grains. It was repeated to the extent of twenty grains during third and fourth remissions. The fifth exacerbation occurred as usual, and no quinia was given, but, notwithstanding, complete defervescence occurred abruptly.

CASE IV. *Double Tertian Remittent* (Chart 8).—E. P——, aged sixteen. First paroxysm at 7 A.M. Exacerbation at 2 P.M.; on fifth day at 9 A.M., after which defervescence was complete. Quinia twenty-four grains was given during each remission.

The following cases are reported by Colin, in his valuable work, to which such frequent reference has been made:

Bilious Remittent Fever.—T——, *ouvrier d'artillerie;* in Rome two years; has been constantly stationed at Fort Sainte-Ange. Was attacked suddenly during the night of August 15, 1864, with persistent vomiting, and the following morning was sent to the hospital of Saint-André, and admitted to my wards (No. 163).

At my visit on the morning of August 16th the sclerotica were of a yellow color, as well as the tongue and the matter vomited; pain on pressure over the epigastrium—far more than in the right hypochondriac region, where percussion does not denote an increase in the volume of the liver. Urine scanty, very yellow. Intense fever; pulse 116; respiration excited. The cephalalgia is so intense as to cause the patient to cry out, and is aggravated by the constant nausea. *Prescription:* Seidlitz water.

Evening visit: slight relief after very abundant bilious stools and vomiting. *Prescription:* eight decigrammes (12 grains) of sulphate of quinine and a potion containing ether.

August 17th.—Notable amelioration; the pulse has fallen to 90, the skin is covered with moisture; icterus more apparent than last evening; several bilious stools during the night; epigastrium not tender. *Prescription:* six decigrammes (about 9 grains) of sulphate of quinine at once; then calomel fifteen decigrammes.

August 18th.—After a tolerably calm night the bilious vomiting has just recommenced; the temperature is augmented; the pulse has gone up to 104; and a violent pain, increased by pressure, is experienced in the left supra-orbital region. *Prescription:* Two grammes of powdered ipecac (about ʒ ss.). At the evening visit there was a notable remission; eight decigrammes of sulphate of quinine and an antispasmodic potion.

August 19th.—A little appetite; liquid alimentation commenced (*bouillon*). The patient was discharged September 1st.

Bilious Remittent Fever.—B——, private Seventy-first Infantry; in Italy three years; not previously in hospital. This soldier has been in garrison for four months at Ceprano, and experienced there, at the end of August (1864), three paroxysms of quotidian intermittent fever. Still a little feeble from this attack he was sent to the military hospital in Rome, where we found him in our service at our visit September 6th (No. 172).

The patient says he has had chills "in his back" all night, also pain in the limbs, vomiting and diarrhœa. The skin is hot, pulse 120; the cheeks—*pommettes*—violet, almost as if ecchymosed. There is well-marked icterus of the alæ nasi and of the sclerotica; tongue yellow, mouth very bitter; continued nausea and bilious vomiting. The cephalalgia is so intense that the patient holds his head between his hands while making the slightest movement. *Prescription:* Potion containing two grammes of powdered ipecac (about ʒ ss.). The same day at our evening visit the fever had increased in intensity, the eyes were brilliant, and the patient was in a state of constant agitation. Pain radiates from the head to the loins, and the patient's body is partly curved backward, with the head buried in the pillow. The vomiting persists. *Prescription:* Fifteen decigrammes (about 23 grains) of quinine by enema, with tincture of opium; fifteen leeches to mastoid processes.

September 17th.—The patient had a bad night; his skin is now cooler; pulse has fallen to 84; icterus more apparent; vomiting has ceased. *Prescription:* Fifteen decigrammes of sulphate of quinine, with laudanum, by enema.

From this time the febrile movement gradually diminished. The saburral state of the primæ viæ still continued for some days; then convalescence was fairly established, and the patient was discharged September 25th.

The following case we take from the recent work of Sir Joseph Fayrer, to illustrate the tendency to relapse after removal from malarious influences, the persistent character of the febrile phenomena in these cases when left to nature, and the prompt relief afforded by *efficient* treatment:

Irregular Remittent.—C. V——, an officer, aged twenty-six; served in India three and a half years. Had fair health for the greater part of the time He went out shooting in the Canara jungle, and was exposed to the malarious influences of that region after the rainfall in May and June. He appears to have had no decided attack of fever until September 18th, and that followed an attack of cholera on September 10th; had previously had malaise, and probably slight feverish attacks. Shortly after he had an attack of fever, for which he was sent home, and the following is the history of his case after his return, and a very typical and instructive one it is:

The chief points that it illustrates are: the apparently long incubation period, the irregularity of the periodicity, the effects of change to another climate, the influence of fatigue and exposure in this country in exciting a return of the paroxysm, the extreme irregularity of the symptoms, and the power of quinine on a person not affected with any visceral complications. Beyond tenderness and fulness of the spleen there was no visceral complication; the heart and lungs normal; urine free from albumen, but high-colored at times. Bowels fairly regular.

Got a chill on November 22d, hunting. November 23d, 24th, 25th, malaise and slight feverish attacks; had small doses of quinine.

On November 26th, temperature was to 103.5°. Notes do not say if rigor preceded or sweat followed.

November 27th, temperature 103.5°, morning; temperature 101.5°, evening.

November 28th, temperature 102°, morning; temperature 102.5°, evening. Intense neuralgia (head) came on; refused quinine. Morphia injected gave relief; profuse sweating.

November 29th, temperature 102°, morning.

In a few days the fever *abated.* Morning temperature 102.5°, evening temperature 100°; temperature usually lower in the evening, but no regularity in attacks of fever; the *early morning* being the time most free from fever. There were profuse sweats, occurring with the same irregularity.

Nourishment was fairly well taken throughout. Quinine given irregularly, *in doses of two or three grains only* (frequently less).

December 1st.—In the morning temperature 100.5°, pulse 78.

December 2d.—Morning temperature 102.5°, pulse 100.

December 3d.—Morning temperature 101.5°, evening temperature 99.5°.

December 4th.—Morning temperature 100°, evening temperature 101°.

December 5th.—Morning temperature 101.5°, evening temperature 100.2°

December 6th.—Morning temperature 99.5°, evening temperature 99°. This marks the end of this attack. He came down stairs; still had *perspirations*, but no fever. Took small doses of quinine two or three times a day.

Friday, December 9th.—He was quite free from fever in the morning, but temperature rose to 104° in the afternoon, and from this date high and continuous fever lasted until the 13th. Temperature never below 102°, rising to 103.5°, with profuse night-sweats.

On December 13th there was a remission, but of short duration. Fever came and went for the four following days; he was thus much exhausted. (It was at this stage that he came under my observation.)

December 17th, 6 A.M.—Temperature 102.5°. Quinine was given, four grains at 6 A.M., four grains at 9 A.M. Temperature again rose to 103.5°. At noon five grains were given, at 3 P.M. five grains, at 6 P.M. five grains, at 9 P.M. five grains, at midnight five grains.

December 18th, at 6 A.M. five grains, at 10 A.M. five grains. At 10.30 A.M. temperature 99°. Patient completely cinchonized. The quinine was now given less frequently. In the evening, temperature 97.5°. The profuse sweats continued for two nights longer, and five grains of quinine were given twice a day up to December 23d. There have been occasional night-sweats, but the temperature has not exceeded 98° and has been as low as 96°. On the 23d he came down stairs. On the 29th he went out. The appetite is excellent and return of strength rapid; very little aperient medicine required. He is convalescent and is going to the south of England for change. I saw him on January 4th. He was pale and had occasional perspirations, but no fever, good appetite, and strength much improved. Recommended to continue quinine for ten days.[1]

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[1] Op. cit., pp. 118–20.

The following case is from the mémoir of Guéguen, already referred to, which received the naval medical prize (French navy) in 1877.

Tertian Remittent Fever.

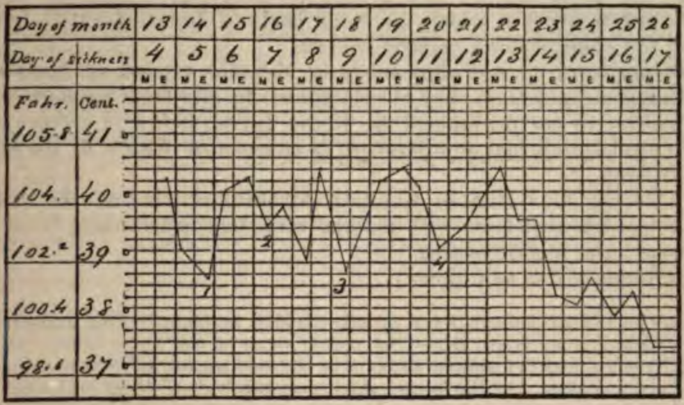

Chart No. 9 (Guéguen).

M. X——, colored, female. Has had fever three days. Two preceding exacerbations. Febrile paroxysm every forty-eight hours, defervescence incomplete. Treatment: Emeto-cathartic at outset, then sulphate of quinine one gramme at each remission (1,2,3, and 4). Cure rapid but great subsequent anæmia.

ARDENT MALARIAL FEVER.

DEFINITION.—A fever produced by the combined influence of heat and malaria[1]; abrupt in its onset, of high grade, and attended by much gastric disturbance; rather continuous than remittent in type. This fever is most frequently met with in tropical countries, but also prevails during the hottest season of the year in subtropical and Southern temperate regions; it attacks by preference unacclimated strangers, and usually does not recur in the same individual while he continues to reside in the tropics.

SYNONYMS.—Inflammatory remittent fever; gastric remittent fever; ardent fever; *fièvre inflammatoire;* summer fever; acclimating fever; common continued fever.

The form of malarial fever at present under consideration differs from simple remittent fever in that heat is an *essential* factor in its etiology. It is this form of fever which Colin has described under the name of "*forme gastrique*" (of the remittent fever of summer), and which constituted the annual endemo-epidemic among the French troops in Rome during the French occupation of that city. In the West Indies it is known as *la fièvre inflammatoire*, and in India as ardent fever, common continued fever, or inflammatory remittent fever. The latter name is that adopted by Morehead, but this author takes pains to explain that "the term inflammatory, as applied to remittent fever, is not to be understood as implying the presence of local inflammation: it is used merely to express a high degree of febrile reaction."

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[1] Presumably the same telluric miasm as that which causes intermittent fevers, but possibly a miasm of a different nature.

ETIOLOGY.—According to Morehead, this form of malarial fever occurs in India "in lately arrived Europeans, in June, July, August, September, and October, months in which, in many parts of India, elevated temperature and the conditions of malaria coexist."[1]

That this fever is not due solely to climatic causes, as many of the older writers supposed, is very clearly shown by the facts presented by M. Colin relating to its prevalence in Rome (given below *in extenso*). But that an elevated external temperature is an *essential* factor in its etiology is also evident.

Dr. Chevers says that to Kenneth Mackinnon "is due the credit of having ranged ardent fever with paludal remittent, attributing them to the same cause—the marsh poison."[2]

Mackinnon writes as follows:

> Authors on Indian diseases have usually divided fevers according to the season of the year at which they occur, thus: the ardent fever of the hot weather, the bilious fever of the rains, and the congestive fever of the cold season. The first and last it is usual to call continued, and the second remittent, although all three may assuredly be produced by the same remote cause. This may be illustrated by the observed effect of exposure in localities (the forests of Singhboom, for instance) where at all periods the miasmatic cause of fever is rife. That heat alone, and especially solar exposure, may cause fever independently of malaria, seems a fact admitted on all sides; but we shall often have difficulty in deciding (when fever is prevalent in the hot months) upon which of the causes the prevalence depends. I have elsewhere alluded to our defective knowledge of the whole conditions essential to the generation of malaria, and I have noticed the fact that it may undoubtedly emit from dry surfaces; nor are we to forget that showers frequently fall in the hot months immediately followed by a hot and dry atmosphere endowed with wonderful evaporating power. It must also be remembered that in some parts of the country even during the hot months there are extensive surfaces which only then are becoming dried up. In these the ardent fever of the hot months will have some character in common with marsh fever; and in seasons when rain falls, according to my observations, the hot-month fevers will be found to exhibit a periodic tendency even in the open localities where our cantonments and civil stations stand.[3]

Colin says with reference to this form of malarial fever:

> The special features of this fever, in particular its continued form and the violence of the gastric troubles, have inspired the thought that perhaps it does not belong to the group of malarial fevers (*affections palustres*)—that it is due simply to meteorological influences of the seasons or of warm climates. The value of this opinion is augmented by the consideration that this disease attacks, above all, the newly arrived, seeming to constitute for them a fever of acclimation, so much the more as after a first attack it usually does not recur.
>
> This was our first impression on arriving in Rome. Seeing remittent fever to appear suddenly (*faire explosion*) with the hot weather, to augment in the number and gravity of the cases with this, to diminish with it; seeing it succeed sometimes insolation, and attack above all the strangers, we asked ourself if it was not due rather to the action of a hot climate than to an influence purely telluric.
>
> This question, then, was one of those which occupied us the most while in Rome, as it had previously occupied our attention in a similar field of observation in Algeria.
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> The importance which I accord to meteorological causes in the genesis of these affections has already been stated. I have even gone so far as to recognize in an elevated temperature the power, almost exclusive, of determining the remittent and con-

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[1] Op. cit., p. 61.

[2] I. Norman Chevers, M.D.: Med. Times & Gaz., Lond., May 8, 1880.

[3] Quoted from Dr. Chevers' paper, op. cit., p. 503.

tinued types, and of proposing the name summer fever (*fièvre estival*) for these affections of July and August; but again I say the elevated temperature gives only the type and does not create the fever itself, which, without the extreme heat, would still exist, only in a periodic instead of a continued form.

The proof that this remittent fever is above all of telluric origin we find in the following considerations:

1. If in Rome it was a climatic affection it would attack the newly arrived immediately, or at least during the heat of the first summer following their arrival. We have seen, on the contrary, that in the immense majority of cases it is not until the third year, when the individual is to a certain extent habituated to the climate, that remittent fever manifests itself. While it appears, then, at the season of greatest heat, it does not result from the action of this agent, which is not new for the subject, but from the degree of intoxication which he has attained, an intoxication which is not sufficiently rapid to develop the fever sooner, at least in the ordinary conditions of a residence in Rome.

2. If this remittent fever arose solely from meteorological conditions, it would attack equally the individuals submitted to the same conditions in this regard. In Rome, for example, it would attack in the same numbers troops situated in the different quarters of the city; whereas, like intermittent fever, it prevails especially among those in barracks situated in the insalubrious and almost deserted portions of the ancient city.

Thus in 1864 a single regiment counted, on August 20th, 143 of its men sick in the hospitals, of whom 137 came from a single battalion lodged in the part of the city mentioned, and six only from another battalion, numerically equal, in barracks in the central and perfectly salubrious quarter of the Convent of *Gesù*.

It is the same in the Roman Campagna, where the localities reputed healthy in the autumn, during the season of intermittent fevers, have also but few sick during the months of July and August. This is the case with Albano, Tivoli, and other places slightly elevated above the plain; while the notoriously malarious localities—Terracine, Orte, Civita Castellana—furnish an enormous number of cases of remittent fever in summer.

3. In 1865 the mean monthly temperature during the entire summer was above the normal mean temperature for these months, yet there was less than one-half as many cases of remittent fever as in 1864, a year in which the spring had been very wet and the summer not so warm as that of 1865.

It is, then, with these fevers the same as with other *malarial* fevers—they are less numerous during exceptionally hot and dry years.

4. When the attack is suddenly developed by insolation, it is in general in an individual previously subjected to a source of malarial infection. . . .

5. In tropical regions where the climatic influences are at their maximum, so far as temperature is concerned, why does not this fever manifest itself among the crews of ships at sea? It is that their essential condition is the action of the soil—of that soil which in hot countries suffices alone to evolve toxic emanations, independently of marshes.

At Civita Vecchia, in 1866, at the moment when the garrison sent me, to the hospital, a great number of cases of remittent fever, this affection respected in an absolute manner the crew of a French ship of war, the Catinat, anchored in the harbor of this city, and consequently subjected to the same meteorological conditions as the garrison, but withdrawn from the sources of telluric intoxication.

6. Finally, in *la Bresse*, in Holland, and in Hungary we encounter these same fevers, without being able to invoke in these countries of the temperate zone the action of climate; for the temperature is not above that of neighboring countries[1] [where these fevers do not prevail, understood.]

M. Colin is undoubtedly mistaken in the generalization he has attempted to make with reference to the non-recurrence of remittent fever in the same individual. No doubt this is true as a general rule with reference to the form of malarial fever under consideration, but the rule does not apply to those forms of malarial disease in which the factor malaria is the most prominent one in the development of an attack. In these cases the periodic character of the febrile movement is more apparent and convalescence is very commonly interrupted by attacks of intermittent fever; whereas in the form of malarial fever under consideration we are informed by Colin that such was not the case.

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[1] Op. cit., pp. 168–171.

We have already referred to the remarkable regularity with which the annual endemo-epidemic was developed among the French troops in Rome during the French occupation of that city—sixteen years. The first cases occurred, *presque à jour fixe*, about July 5th or 6th; the epidemic reached its height by the 20th of the same month, and commenced to decline about August 20th. The movement of decline was so rapid that by the end of August the number of cases was already small, and during September the few cases that occurred were, so to speak, lost in the immense number of cases of intermittent fever.

In India, where the hot weather is more protracted, we are told by Dr. Morehead that the season of prevalence is from June to October. This author gives the following account of the etiology of "inflammatory remittent fever:"

> In robust Europeans, lately arrived in India, exposed to malarious influence and neglectful of the ordinary means of preserving health, remittent fever, with severe exacerbations, is likely to occur, attended with much headache, pain in the limbs, restlessness, flushing of the face, perhaps delirium. The skin is hot and pungent and the pulse full and frequent. A sense of oppression is felt at the epigastrium, accompanied by nausea and frequent vomiting. The tongue is much coated and its edges and tip are often florid. Thirst is urgent and the excretions are scanty and vitiated. The remissions are well marked but they are proportionate to the severity of the exacerbation, so that the febrile state in them may almost equal in degree that of the exacerbation in the mild form of the disease. . . . If to this variety of remittent fever, as now described, the influence of exposure to elevated temperature or of excesses in drinking be added, then that compound form to which I have already alluded —in which the exacerbation is of longer and the remission of shorter duration, and in respect to the classification of which, as continued or remittent, there is often doubt —will be produced.[1]

Bérenger Féraud is of the opinion that the *fièvre inflammatoire* of the French Antilles is a benign form of yellow fever. If so, we are wrong in supposing that the disease which goes by this name in the West Indies is identical with the "inflammatory remittent" or "ardent fever" of India. We cannot doubt, however, that the influences which produce the form of disease under consideration are in operation in the West Indies and in tropical America generally, as well as at Rome or in India; and as similar causes produce similar results in all parts of the world, it seems unnecessary to invoke another etiological factor—and one which ordinarily produces very different results—to account for the prevalence of a non-fatal form of ardent fever among strangers visiting the West Indies during the hottest portion of the year.

The opinion of Féraud is, however, entitled to very great consideration, and we are not prepared to deny the possibility that the yellow fever poison in attenuated form may, in regions where this disease is endemic, form the basis of an attack of *ardent fever*, of which the exciting cause is exposure to heat, and which is identical in form, although not in etiology —so far as the remote cause is concerned—with the "inflammatory remittent fever" of the East Indies.

DIAGNOSIS.—The fact that the initial symptoms in ardent malarial fever are similar to those of yellow fever and that the pyrexia is of a continuous rather than of a remittent character, makes the differential diagnosis difficult, and in many cases impossible at the outset of an attack. But the same is true with reference to other specific diseases—*e. g.*, small-pox or dengue. Later, however, the diagnosis may commonly be established by the presence or absence of the symptoms peculiar to these diseases—eruptions in small-pox or dengue, albuminous urine, hemorrhages, etc., in yellow fever.

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[1] Op. cit., p. 61.

The benign character of the disease under consideration also aids in distinguishing it from yellow fever. It is true that the latter disease sometimes prevails in a comparatively mild form, but the very mildness of the initial symptoms will in this case assist in the diagnosis, for ardent malarial fever is always violent in its mode of attack. In yellow fever, on the other hand, the initial symptoms often give no evidence of the malignant nature of the disease. Frequently there is no gastric disturbance at first and very little cephalalgia or lumbar pain; and on the third or fourth day the patient considers himself convalescent and desires to get up and to have "something to eat," when the experienced physician knows that the slightest imprudence of this nature might give rise to suppression of urine, black vomit, and death.

The fact that sporadic cases of ardent malarial fever and of yellow fever are both likely to occur among strangers in the regions where the latter disease is endemic, naturally gives rise to much confusion and to errors in diagnosis, and probably no amount of skill is sufficient to prevent such mistakes in certain cases. The different etiology of these two forms of fever is made very apparent when they prevail epidemically.

In the one—ardent malarial fever—the exciting cause being climatic and the remote cause being wide-spread, the outbreak is sudden, and cases occur simultaneously among the susceptible individuals in an extended territorial area, as in Rome during the French occupation: in the other the disease is at first limited to certain infected centres, and from these it spreads—often in a most deliberate manner—attacking susceptible individuals as they come within the extending area included in its progress, while those outside this area remain in perfect health although subject to the same climatic conditions. Moreover, in those regions which are only occasionally invaded the disease may be traced to importation, and there is often a considerable interval between the arrival of an infected vessel or the landing of infected goods or imported cases, and the occurrence of cases of local origin as a result of such importation.

PROGNOSIS.—No doubt complications of a fatal character may occur in this as in other forms of malarial fever. But during the annual endemo-epidemic among the French soldiers in Rome a vast majority of the cases were uncomplicated, and they all presented a remarkable uniformity in their clinical history and were of an extremely benign character, notwithstanding the apparent gravity of the initial symptoms. M. Colin says that convalescence was generally established without check and without the occurrence of attacks of intermittent fever. "But whatever may have been the care taken or the remedies employed, these convalescents did not leave the hospital with the attributes of their former state of health; they were pallid and had the complexion of the ancient residents," and were extremely susceptible to atmospheric vicissitudes and to contract intermittent fever.

SYMPTOMS.—The following account of the clinical history of these cases is given by the author from whom we have already quoted so extensively, and whose observations with reference to this form of disease are especially valuable, both on account of his extended experience and because his field of observation was one in which the confusion which elsewhere might have resulted from the simultaneous prevalence of yellow fever, of relapsing fever, or of dengue, was not likely to occur. We may remark here that a perusal of the account given by M. Colin of this "gastric form" of remittent fever leads us to suspect that many cases of the same character, occurring in the West Indies and in the southern portion of our own country, have frequently received a different name and have been classed as dengue :

> In the midst of the most perfect health, at least in a majority of the cases, the patient is seized with violent cephalalgia, accompanied by pains in the loins and limbs, and in a few hours presents the symptoms of the most intense fever. The skin is hot and burning ; the pulse 110 to 120 and resistant ; the respiration anxious, the face and conjunctivæ congested ; thirst intense ; the urine red. Ordinarily there is no initial chill, or it is less intense than in intermittent fever and is not repeated during the course of the disease. The tongue is white or colored yellow by the bilious vomiting which frequently marks the onset of an attack. The epigastrium is tense and vaguely painful on pressure ; there is but little augmentation of hepatic dulness ; constipation is the rule.
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> During the night there is an exaggeration of the cephalalgia, of the pain in the limbs, and of the agitation. Sometimes there is delirium. Ordinarily the patients feel slightly better in the morning, although no great diminution of the pulse or of the temperature can be observed.
>
> The symptoms which yield first are the febrile phenomena ; almost always there is a notable amendment toward the third or fourth day ; the gastric symptoms are the most persistent. The appetite usually does not return in less than a week, and the violent shock of the nervous system lasts still longer ; the patients remain feeble, and I have even seen paraplegia consecutive to this benign form in two instances. Aside from these exceptional cases the regularity of the morbid evolution is such that the cases resemble each other, so to speak, from day to day ; that in nearly every case the disease is inaugurated, progresses, and declines with a regularity which we cannot ascribe to the uniformity of the treatment. Many times it has happened to us to discharge together groups of ten, fifteen, or twenty individuals who had been admitted to the hospital the same day.
>
> The mean duration of their stay in my wards was from fifteen to twenty days, of which the last eight were devoted exclusively to the establishment of convalescence by supporting treatment. . . .
>
> We see from these examples [cases reported below] that the clinical characters of this fever are : First, its inflammatory appearance (*allure inflammatoire*); the patients attacked for the first time, and until then enjoying the plenitude of their strength, have not the complexion which belongs to individuals attacked by the more advanced forms of malarial intoxication. Second, the intensity of the lumbar, epigastric, and cephalic pains, which, with the vomiting, anxious respiration, injection of the conjunctivæ, and vultuosity of the face, constitutes a group of symptoms analogous to those of the first stage of yellow fever and of the invasion of variola of a grave form. Third, the frequent absence of an initial chill—which has given rise to the name "*fièvre chaude*," commonly given to this affection. Fourth, the daily paroxysms are not usually preceded by a cold stage, and the evening febrile exacerbation does not exceed the limits observed in other febrile diseases.
>
> We see how much this fever differs clinically from intermittent. In the greater number of cases it offers nothing which resembles periodicity, and if we have more frequently called it remittent than continued, it has been in order to conform with the use of terms generally adopted—a usage perhaps to be regretted, for the word remittent is, in our opinion, a vestige of the tradition which has imposed upon these forms of fever a periodic character, although they are essentially continuous. We believe that this fever would be more properly designated ardent fever, *fièvre chaude*, or summer fever, than by a name which helps to preserve an erroneous belief in its periodicity.

No doubt cases of this form of malarial fever are common enough in the southern portions of the United States during the summer months, and we believe that the remittent fever referred to by Maury as frequently met with in the Lower Mississippi Valley, in which defervescence occurs suddenly on the third or fifth day independently of the use of quinine, is identical with that which has just been described.[1]

TREATMENT.—This form of fever, which occurs in sthenic individuals and usually in those who have recently arrived in the regions where it prevails, is attended with symptoms of a character which were formerly supposed to demand active antiphlogistic treatment; and accordingly the older physicians resorted to general bleeding, purging, leeching, antimonials, and mercury. Fortunately the discovery was made that patients not only recovered without this heroic treatment, but that the proportion of recoveries was greater and convalescence was more rapid and more complete when it was not resorted to or was employed in a greatly modified form.

In India, Mackinnon was among the first to admit that "there are many cases of ardent fever in which bleeding may be dispensed with." Still he says that "it is in this type of fever that we may use the lancet with the greatest freedom and safety," and his general treatment consisted in bleeding and the administration of purgatives, sedatives, and mercury until the febrile symptoms disappeared, when he ventured to prescribe quinine. Chevers says that a perusal of the pages written by this author relating to the treatment of ardent fever affords an admirable example of an original but most cautious mind struggling to free itself from the trammels of tradition and authority.

Dr. Morehead, who perhaps did more than any one else in India to establish the therapeutics of malarial diseases upon a rational basis, still made some concessions to venesection, and the local abstraction of blood by leeches applied to the epigastrium or to the mastoid processes is recommended for the relief of congestion. He says:

> In the treatment of inflammatory remittent fever freer depletion is required, but still it should be used with watching and caution, and the safest time is at the height, not the close of an exacerbation. Nor should we forget that evacuants are had recourse to, not in the hope of cutting short the attack, but merely of lessening the risk of injury from vascular excitement, and that they are being used in a disease which, if it persists, is sooner or later sure to terminate in signal depression of the vital actions. The best guide to the successful application of depletory remedies is the presence of a dry skin, of steadily increased temperature, and a pulse frequent, firm, and of good volume, associated with hyperæmia of an important organ.

Even the cautious use of venesection permitted, rather than recommended, by Morehead is generally condemned by more recent authorities. Thus Fayrer says: "The high fever, racking headache, muscular pains in the back and limbs, epigastric pain, nausea, vomiting, and other painful symptoms, call urgently for relief, but not by bleeding, *unless indeed a few leeches be applied, and that but very seldom*."[2]

Chevers says:

> Those who treated Indian fever by blood-letting committed disastrous havoc by the fatal error of treating that mere name "ardent fever," instead of that true entity the "paludal intermittent of the hot weather" [our ardent malarial fever].
>
> I never had recourse to venesection in any case of Indian fever, however severe the head symptoms might be. In one case, soon after my arrival, I applied leeches to the temples. I felt convinced that they did no good, and I never considered it needful to employ this treatment again.[3]

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[1] See his paper referred to, Am. J. M. Sc., April, 1882.

[2] Op. cit., p. 109.

[3] Op. cit., p. 502.

It would seem from this that in Indian practice leeches are in a fair way to follow the lancet, inasmuch as one high authority—Fayrer—merely permits their use in exceptional cases, and another practitioner of extended experience—Chevers—finds that he can dispense with them entirely. In this country we believe that they are rarely used, although we still find them recommended by some authors for the relief of local congestion. It is difficult, however, to find an anatomical reason for applying them to the epigastrium, as is commonly recommended, when the object in view is to relieve a hyperæmic condition of the mucous membrane of the stomach.

If we reject depletion, which in the hands of our predecessors undoubtedly did afford very great relief to the distressing symptoms which attend the first stage of ardent malarial fever, what shall we substitute for it? We have no hesitation in answering, the same remedies as have been recommended in other forms of malarial fever, and especially cold water and quinine; the latter to be given as an antipyretic rather than as an antiperiodic remedy. If we were obliged to choose between the two it might be a question which to select, for quinine is not essential for the cure of this form of fever, which seems to have a tendency to terminate spontaneously by sudden defervescence attended with perspiration at the end of four or five days. But in a full sedative dose it seems probable that quinine will be found to act favorably in reducing the temperature and relieving the nervous symptoms in this as well as in other forms of fever—*e.g.*, in thermic fever, or in enteric fever. It will be useless, however, to give it in small and repeated doses with a view to neutralizing the malarial element in the disease. This will but add to the headache and gastric irritability without reducing in a material manner the degree of pyrexia. Without claiming any personal experience in the use of large doses in ardent fever of this character, we should confidently anticipate extremely favorable results from the administration by hypodermic injection of ten to fifteen grains at the outset of the attack, or of an equivalent quantity by enema—forty to sixty grains—to be repeated in twenty-four hours if necessary. This, however, is not suggested as a substitute for the cold-water treatment, which is perhaps our most valuable therapeutic resource in this form of fever. To be efficient it must be faithfully and persistently applied, either by the use of cold baths, cold affusions, or sponging the surface at frequent intervals with ice-water. In severe cases an ice-cap should be applied, but ordinarily large compresses wrung out of ice-water applied to the head and trunk, and the occasional sponging of the extremities with cold water or an evaporating lotion, will suffice to keep the pyrexia within bounds and to relieve the intense headache. Swallowing bits of ice, or small quantities of carbonic acid water as cold as ice can make it, will serve better than anything else to allay the vomiting, and if this does not answer it is useless to try one after another the list of remedies which have been recommended for this purpose. Relief will often be afforded, however, by the application to the epigastrium of a sinapism, or a little chloroform applied upon lint and covered with oiled silk to prevent evaporation. In general it will be found that local hyperæmia and pain in any of the organs will be more readily relieved by the external application of rubefacients or of cold compresses than by internal medication. Emetics and antimonials are in general contraindicated from the tendency to gastric irritability which exists (Morehead), but the refrigerant diaphoretics may be given as recommended in the article on "Simple Remittent Fever."

It is generally considered necessary that the bowels should be freely moved at the outset of an attack, but care must be taken in selecting a cathartic for this purpose, for drastic and irritating purgatives do far more harm than good. Morehead says:

> Though to increase hepatic and intestinal excretion, with the view of lessening febrile reaction by evacuation and of removing the products of augmented metamorphosis of tissue, is a distinct indication, yet we are frequently obliged to be very cautious in the use of calomel and purgatives, for there is often present congestion of or determination to the gastro-intestinal lining, very apt to be increased or to pass into inflammation by the use of irritants and thus to aggravate the fever.

It is worse than useless to administer nauseous cathartic medicines when the stomach is already in a state of rebellion and is sure to reject them. In this case a purgative enema may be given, or the bowels may be left to the care of Dame Nature, inasmuch as they are not responsible for the febrile attack and no amount of purging will relieve it. If, however, the bowels are confined, and the stomach is in a condition to retain it, a full dose of castor-oil may be given. This is a favorite prescription at the outset of an attack of this kind in the West Indies, and has the advantage of being both prompt and efficient in its action and at the same time harmless. Or, if preferred, a saline cathartic may be administered—*e.g.*, a dose of sulphate of magnesia or of Hunyadi Janos water.

CASES.—The following cases are reported by Colin:

> *Gastric Remittent Fever.*—B——, private Fifty-ninth Infantry; in Italy two years; not previously in hospital; stationed in the quarter Saint-Esprit; admitted to hospital July 14, 1864.
>
> Was seized suddenly on July 12th with violent cephalalgia, which still persists; had some irregular chilly sensations and vomiting of food.
>
> To-day (July 14th) at the morning visit his face is deeply flushed, pulse 120, skin hot. Had a greatly agitated night, owing to the intolerable pain in his head, back, and limbs; urine very red and of high specific gravity. Tongue broad and white; epigastrium tense, slightly painful; constipation. An emetic had been administered before his admission to hospital. *Prescription:* Seidlitz water; eight decigrammes (about twelve grains) of sulphate of quinine to be given at three o'clock.
>
> July 15th.—Headache and fever have diminished, skin moist, tongue still white, no appetite. *Prescription:* Seidlitz water; five decigrammes of sulphate of quinine at three o'clock.
>
> July 16th.—Face pale, skin cool; pulse has fallen to 78; the patient has some appetite and complains only of extreme feebleness, which prevents him from sitting up in bed. *Prescription:* Bouillon and stewed prunes; five decigrammes of sulphate of quinine.
>
> The following days the appetite rapidly improved and convalescence was established without check, the patient being discharged from hospital July 29th, and having then been on full diet for three days.
>
> *Gastric Remittent Fever.*—P——, private Twenty-ninth Infantry; in Italy six months; not previously admitted to hospital; stationed in the quarter of Cimara; admitted to hospital (Saint-André) July 22, 1864 (No. 117).
>
> Had a chill last evening, followed by so violent a headache that he cried out with pain during the entire night. At the moment of my visit (July 22d) his face was red and animated, his eyelids swollen, and conjunctivæ injected; skin dry and burning; pulse hard and full, 116. Tongue yellow; bilious vomiting; violent pain in the head and limbs, as in the period of invasion of variola. *Prescription:* Potion containing two grammes of ipecac.
>
> The same day at the evening visit the symptoms still persisted. *Prescription:* Twenty leeches to mastoid processes, and one gramme of sulphate of quinine.
>
> July 23d.—The patient has been very restless and has vomited all night; but is comparatively calm at the time of the visit; pulse 100; skin hot, without moisture. One gramme of sulphate of quinine was administered in our presence and was retained.
>
> At the evening visit the heat was greater, pulse 110, tongue dry; persistence of the constipation. *Prescription:* Five decigrammes of sulphate of quinine and a purgative enema.
>
> July 24th.—Apyrexia almost complete; skin moist, face pale, tongue still very white and saburral; an extreme feebleness has replaced the agitation of the preceding days;

voice almost extinct. (Bouillon, an egg, wine, and a potion containing six grammes of acetate of ammonia.)

July 25th.—Gradual amelioration; appetite improved (quarter diet; potion containing six grammes of extract of quinquina). From this time the diet was gradually augmented and the patient was discharged August 15th.

The following cases, which we think are properly included under the heading "ardent malarial fever," are taken from the valuable paper by Maury, already referred to:

CASE V.—*Pernicious Remittent* (Chart No. 10).—H. M——, male, aged eleven years; attacked June 10th. Invasion between midnight and daylight. He was attacked very violently with fever, headache, backache, extreme restlessness, and uncontrollable vomiting, at first of bile and afterward watery mucus. Irritability of stomach continued until subsidence of the fever on the fifth day, to such an extent that even the smallest quantity of milk with lime-water was rejected. No perceptible remission occurred until the third day. Defervescence was sudden and complete on fifth day. No quinia was given and no medicine of any kind, except three grains of calomel, which were administered before I saw him. This acted upon the bowels several times. The cold-water treatment was vigorously and unremittingly used, by means of sponging the surface with iced whiskey and compresses wrung out of ice-water covering the front and back of the trunk. During this attack the pulse ranged from 120 to 150. Delirium was constant. Convalescence was rapid.

CASE VI.—*Quotidian Remittent of Eight Days' Duration* (Chart No. 11).—B. H——, aged two years, a delicate, nervous girl. Nausea and great restlessness marked the invasion. Quinia, eight grains, was given at 12 M. on third day. This was in part rejected. Quinia, sixteen grains, was given by enema at 11 P.M. on the fourth, but was in part rejected. It was repeated with same result on the fifth night. Soon afterward nine grains were given by the mouth and retained. At 11 P.M. on the sixth ten grains of quinine were given by mouth. The cold-water treatment was used as in the last case.

Two features in this case should be noted: First, the complete intermission which occurred at the close of the fifth day, though quinia had been given so unsatisfactorily and ineffectively; second, the abrupt termination of the fever at the close of the eighth day, the thermometer sinking at midnight to 96° and the pulse falling to 80, being very feeble and irregular, and requiring the administration of brandy and broth and the rubbing of the body with dry mustard. No medicine of any kind had been administered since 11 P.M. on the sixth day.

Dr. Maury says:

> These cases have been selected from my records as illustrating the natural tendency of this fever, when aided by appropriate treatment, to terminate by crisis on the fifth day. I might multiply them without number if it were necessary. Such was the rule with the fevers of lower Mississippi. Such has been the rule of those of West Tennessee. Very rarely have I found them running to the seventh and ninth days.

In the temperature charts given by Guéguen of *fièvre inflammatoire* as it occurs in the French Antilles, we find that the pyretic movement had a similar character, and that after a continuous high fever of four or five days' duration there was abrupt defervescence on the morning of the fifth or sixth day. This was commonly followed by a second period of febrile reaction lasting two or three days, in which the degree of pyrexia was much below that which characterized the initial paroxysm. We find the same characters in charts given by this author representing the forms of remittent fever denominated by him *fièvre rémittente bilieuse* and *fièvre rémittente simple*.

It will be seen that the second period represented in Dr. Maury's chart (No. 11) resembles that in the chart (No. 12) of *fièvre inflammatoire* given by Guéguen, but that the febrile exacerbation reached a considerably greater height and the daily remissions were more distinct.

This tendency to defervescence on the morning of the fifth day has also been observed by the writer in yellow fever, and while it is far from being a general rule, it has been observed in a sufficient number of cases to give some significance to the fact, and to show that the differential diagnosis of ardent remittent fever and yellow fever cannot rest upon the character of the pyrexia alone. In our cases of yellow fever, however, the defervescence was usually a gradual one, extending over a period of three or four days, or from the very outset of the attack, the acmé of temperature being reached in a few hours; whereas in the six charts given by Guéguen of *fièvre inflammatoire*, defervescence is in every instance abrupt and occurred

Pernicious Remittent.

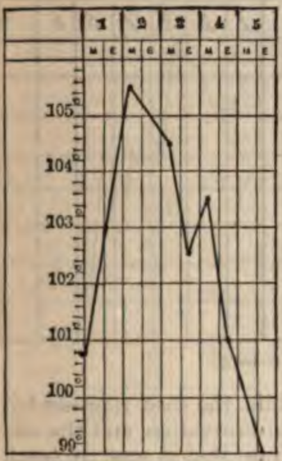


Chart No. 10 (Maury).

Quotidian Remittent.

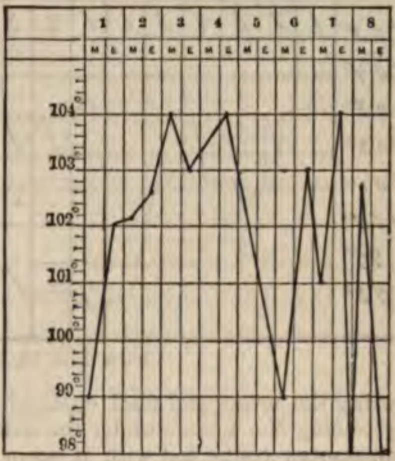


Chart No. 11 (Maury).

Fièvre Inflammatoire.

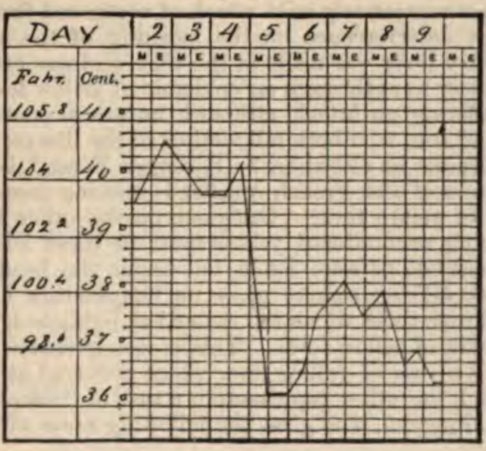
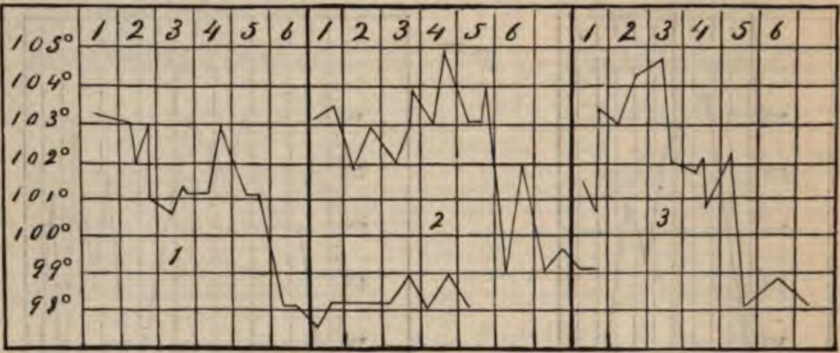


Chart No. 12 (Guéguen).

in the course of a single night.[1] But three of our yellow fever charts[2] exhibit a like abrupt defervescence, and the question will at once arise whether these do not represent mistake in diagnosis rather than yellow fever. We give the charts referred to below, and remark that tracings Nos. 2 and 3 represent cases which occurred at the Pensacola Navy Yard

Yellow Fever.



Charts Nos. 13, 14, and 15 (Sternberg).

during the severe and fatal epidemic of 1874, while the case represented by tracing No. 1 came under the writer's personal observation, and the circumstances connected with it seem to demonstrate that it was in truth yellow fever. The case was that of an officer who exposed himself to the infected area in the vicinity of the Pensacola Navy Yard (village of Warrington) when the epidemic at that place had terminated for want of material. He had a comparatively mild attack of continued fever, which terminated by abrupt defervescence on the morning of the sixth day. The diagnosis of yellow fever was made at the time, and was established by the fact that this officer went through an epidemic of yellow fever the following year without suffering an attack, although he was in constant attendance upon his wife and son, who both fell victims to the disease. But may not the error in diagnosis lie elsewhere? Bérenger Féraud believes that the *fièvre inflammatoire* of the French Antilles is nothing more nor less than a benign form of yellow fever. Guéguen, on the other hand, makes no mention of having encountered yellow fever in these islands, where his temperature observations were made, but under the heading simple bilious fever (*fièvre bilieuse simple*) gives us temperature charts which are almost identical with those which the writer has published,[3] and which represent typical cases of yellow fever. This is seen in charts Nos. 16 and 17, one representing a case of yellow fever which occurred at Fort Barrancas, Fla., in 1873, and the other representing a case of "simple bilious fever" (?) reported by Guéguen, who gives the following notes of the case:

P——, aged forty-two years, sapper Second Regiment Marines.
A. Muscular pains, fever, nausea, bilious vomiting.
B. Prescribed pulverized ipecac, two grammes; sulphate of quinine, one gramme.
C. Slight sub-icteric tint of conjunctivæ. Sulphate of soda, forty grammes.
Remark.—The muscular pains persisted a little longer than usual.

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[1] Op. cit., Plate II., p. 105.

[2] See paper in Am. J. M. Sc., July, 1875, on The Nature and Duration of Yellow Fever.

[3] Am. J. M. Sc., July, 1875.

If it were not for the bilious vomiting this might pass for a mild case of yellow fever. If it was truly "simple bilious fever," and the defervescence occurred as a result of the emetic of ipecac and fifteen grains of quinine administered on the third day (at B.), we can only say that these

Yellow Fever.

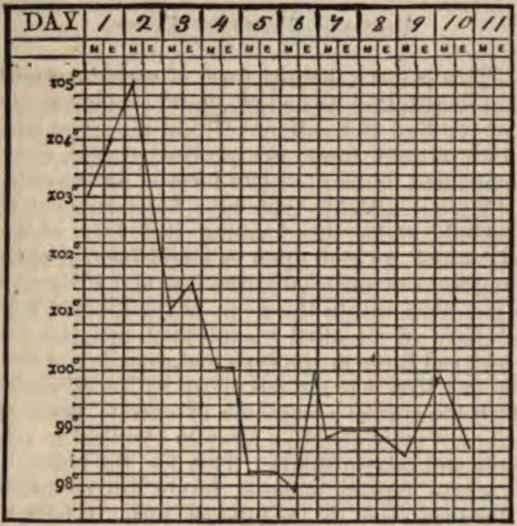

Chart No. 16 (Sternberg [1]).

Fièvre Bilieuse Simple.

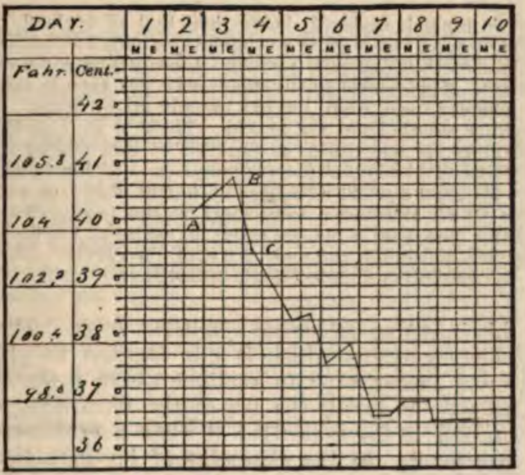

Chart No. 17 (Guéguen).

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[1] No. 11, Plate II. of paper in Am. J. M. Sc. of July, 1875 (Dr. S——)—case at Barrancas, Fla., 1873.

cases yield more promptly to treatment in the Antilles than they usually do in this country, and that the temperature curve is so similar in the two diseases as to furnish no material assistance in making a differential diagnosis.

ADYNAMIC REMITTENT FEVER.

DEFINITION.—This is not a distinct form of malarial remittent fever, but for convenience of description we include under this heading a class of cases which, instead of yielding to treatment within the usual time or terminating in simple intermittent fever, are protracted and develop adynamic symptoms, accompanied by more or less fever of an irregular character.

SYNONYMS.—Fièvre rémittente typhoïde ; fièvre subcontinue estival.

We do not include under this heading that form of fever known as "typho-malarial," which we look upon as a mild form of enteric fever complicated with symptoms of malarial poisoning, and a description of which, therefore, does not come within the scope of the present volume. Nor do we include that form of so-called "continued malarial fever" which resembles typho-malarial fever in the type and duration of the febrile movement, and in the fact that it is not cut short by the administration of quinine, but in which the special symptoms of enteric fever are obscure or absent; for we do not recognize this fever as identical in etiology with the paludal remittents and intermittents. This for the reason that it is often quite prevalent where typical malarial fevers are comparatively rare or unknown, and because even in its mildest form it fails to yield to the treatment by which the most intense forms of malarial toxæmia—pernicious malarial fevers—are commonly cured.

Of this "malarial continued" fever Dr. Maury says:

> Its thermometric range is decidedly lower than that of typhoid. It seldom goes above 103½°. Vomiting of bile is quite a common symptom during the first days of the attack. Bronchial catarrh is generally present. Constipation and a concave abdomen are marked features. Appreciable splenic tenderness has been so rare in my observation that from memory I can recall but two cases in fifteen years. All the essential features of typhoid or enteric fever are absent. There is no diarrhœa, no ileo-cæcal tenderness or gurgling, no meteorism, no eruption of rose-colored spots. As a rule, there is entire absence of abdominal symptoms. . . . This fever presents a stadium of increase of about a week, a stadium of height of five or six days, and a stadium of decrease which terminates completely on the twenty-first day. . . . I am well satisfied that this fever is not the result of neglected remittent, as some have intimated. It begins, continues, and ends as a continued fever. Its duration is in no way affected by the exhibition of antiperiodic remedies.[1]

Evidently this is not an *adynamic* remittent fever. There is nothing in the clinical history given—which is one familiar to physicians in all parts of the United States, even in sections where malarial intermittent fevers do not prevail—to justify the use of the term adynamic as applied to it. It is *continued* in the sense that it runs a protracted course independently of treatment. In the character of its pyrexia, however, it is often more decidedly remittent than malarial "remittent fever" (see Dr. Maury's Chart No. 7). But is it malarial? This depends upon the meaning which is attached to the term malarial.

If the word is used in its broadest sense as indicating that a disease said to be malarial is caused by respiring an atmosphere contaminated by noxious telluric emanations of any kind, then it seems altogether probable that this fever is malarial. But in the restricted sense in which the word is used in the present volume we cannot consent so to call it; for we find it difficult to believe that the same malaria which produces intermittent fever is concerned—directly and primarily—in the etiology of a disease having a clinical history so essentially different.

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[1] Op. cit.

ETIOLOGY.—The distinction between simple remittent fever and adynamic remittent fever is made for clinical purposes only, and the etiology being the same, we have only to inquire here, To what are the adynamic symptoms to be attributed?

Morehead answers this question as follows:

> To the intensity of the cause; to the greater amount of febrile excitement consequent upon the fever having become continued; to the previous influence of predisposing causes, as insufficient food, lengthened exposure to hot weather, intemperance, depressing passions, bodily fatigue, or previous disease Or they may arise from medical treatment having been neglected at the commencement, or from its having been too depressing in character—too much general blood-letting, leeching, antimony, calomel, catharsis, and the neglect of quinine and nourishment. When several of these conditions coexist—as intense malaria, predisposition, and injudicious medical treatment—then are combined the conditions most calculated to produce a fever of a highly adynamic and malignant character.[1]

This answer is so comprehensive and comes from so high an authority that there is little to add to it, but we place beside it a quotation from one of our highest American authorities. Professor Wood says:

> Bilious fever is sometimes of a low, adynamic, or typhous character from the commencement. This may be the result of a previous exposure to causes calculated to depress the vital powers and to deprave the blood; but it probably most frequently arises from the co-operation of a typhoid epidemic influence with miasmata.

We remark that if "typhoid epidemic influence" means anything in this connection it must mean the presence of the special poison of typhoid or enteric fever, inasmuch as the distinguished author quoted refers to "causes calculated to depress the vital powers and to deprave the blood" as something distinct from the typhoid epidemic influence. Since Professor Wood wrote the lines quoted, cases coming under the latter category are recognized as typhoid or "typho-malarial" fever, and are no longer included under the heading adynamic remittent fever. No doubt, also, the number of cases properly so-called has greatly diminished since physicians have learned to administer quinine freely without waiting for a remission, and thus to abridge the duration of an attack, and since quinine and cold water have replaced the lancet, antimonials, and a mercurial course in the treatment of remittent fever. Under this more rational treatment, also, those complications to which the protracted course of a remittent fever is frequently due may often be avoided; and the secondary blood-poisons, which give it an adynamic character, are formed in less amount as the duration and intensity of the pyrexia is greatly modified by the treatment—or if formed are more promptly eliminated as the gastro-intestinal mucous membrane is better able to perform its excretory functions—which it cannot do when in an intensely hyperæmic condition, whether this be a result of the paralyzing influence of the malarial poison or is induced by the irritating action of cathartic medicines injudiciously administered.

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[1] Op. cit., p. 63.

If a primary attack of "bilious fever" is less likely to assume an adynamic type under the improved treatment of the present day, we have still to contend with those predisposing causes which "depress the vital powers and deprave the blood," and chief among these, as being most widely diffused, we must place the malarial poison itself. Victims of malarial cachexia who from fresh exposure or as a result of secondary causes are attacked with remittent fever, have less resisting power to the effects of malaria, less susceptibility to the curative action of quinine, and more or less damaged excretory organs. They are therefore more subject to the development of adynamic symptoms. The same may be said of those who have fallen into a cachectic condition from any other cause, as for example from the influences which produce scurvy or from crowd-poisoning. The exposure of individuals in a depraved state of health from any of these causes to malaria in an intense form may give rise to those fatal forms of fever which some of the older writers called *putrid* remittents. Maclean says in regard to these:

> The medical officers of the first expedition to China, in the year 1840, had an opportunity of observing, under the unsanitary arrangements which characterized so conspicuously the first occupation of Chausan, the terrible effects of malaria and scorbutus combined. An entire regiment, nine hundred strong, was almost destroyed by malarious fevers and bowel complaints in a few weeks, and such of us as survive can bear testimony to the truthfulness of the description of the "putrid" remittent fevers given by the writers above alluded to.

Maclean also recognizes a form of remittent fever which presents adynamic symptoms from the outset, independently of the scorbutic taint. He encountered such cases while serving in the vicinity of the city of Hyderabad in the Deccan.

> From the malarial quarters of that densely populated and most unsanitary city, I used to receive into the Residency hospital during the autumnal months a number of cases of this kind, presenting from the first signs of great depression, the fever after the second or third exacerbation becoming almost continued, the skin being yellowish and covered with petechiæ, the pulse exceeding 120, small and compressible, the tongue dry and black, the teeth covered with sordes, the respiration quick and sometimes irregular, the abdomen distended, the bowels loose, and a disposition to hemorrhage from nose, mouth, and bowels, and almost invariably delirium, with a tendency to coma. Such cases, unless energetically treated, hasten rapidly to a fatal termination by exhaustion and coma.

We remark that this history is so different from that of uncomplicated cases of malarial fever, that, without denying the influence of the malarial factor, we suspect that it plays an inferior rôle in the production of these adynamic fevers, and that they are in truth "putrid" fevers, in the etiology of which the unsanitary surroundings of these denizens of the populous Indian city referred to was the leading factor.

The observations of Colin, made in Rome, show that the adynamic remittent fevers of that city, which seem not to have differed materially in their clinical history from the cases above described by Professor Maclean, proved frequently at the autopsy to present the pathological lesions of enteric fever. M. Colin says with reference to this fever, called by him *fièvre subcontinue estivale* (*ataxique, typhoide, remittente typhoide*):

> This affection, which in Rome as in Algeria manifests itself almost exclusively at the season of the greatest heat, may be developed in the course of an intermittent fever, but attacks above all individuals having simple remittent fever.
>
> Its existence is established by the prolongation of the duration of this remittent

fever, by a very notable aggravation of all the symptoms, by the appearance, in short, of a train of morbid phenomena which cannot be better summarized than by the title "typhoid state." This transformation is characterized by an augmentation of the nocturnal delirium, by the tendency of this delirium to become continuous, by muscular trembling, dryness and sordes of the tongue, meteorism, epistaxis, sudamina. In short, aside from diarrhœa, which is not constant, we find in these patients the principal features of our typhoid fever, especially in its ataxic form, the most rapidly fatal of all.

That which gives to this question a special interest is that in addition, in some of the cases, we find at the autopsy the lesions of typhoid fever, and in their most pronounced forms; while in others, on the contrary, the autopsy reveals only the lesions of the pernicious fevers.[1]

There seems to be no escape from the conclusion that a fever which presents the symptoms and pathological lesions of typhoid fever is true typhoid, although it may have commenced as a simple remittent. But what shall we say of the cases which present the same symptoms and terminate in the same way, but in which the intestinal lesions of enteric fever are absent? We must either confess our inability to make a differential diagnosis between adynamic remittent fever and enteric fever from the clinical history alone, or we must admit that typhoid fever may exist as a complication of simple remittent without the presence of the characteristic intestinal lesions of this disease, or that the anatomical lesions supposed to be peculiar to enteric fever may be developed in simple remittent fever which has assumed the adynamic form.

We are not here concerned with the etiology of enteric fever, but have no hesitation in giving this name to the cases in which M. Colin found the intestinal lesions which accompany this disease, whether they were due to a specific poison or were developed independently of any external agency. The cases in which the integrity of the intestine was verified by a carefully made autopsy, and in which only the lesions peculiar to malarial fevers were found, we do not hesitate to denominate adynamic remittent fever.

DIAGNOSIS.—We recognize the fact that it is often extremely difficult to establish a differential diagnosis between remittent fever in which adynamic symptoms are developed from any of the secondary causes heretofore mentioned, and remittent fever in which similar symptoms occur as a result of enteric complication—specific or secondary.

The differential diagnosis between simple remittent fever having an adynamic tendency in consequence of the cachectic condition of the individual attacked, and uncomplicated typhoid or typho-malarial fever, is also attended with great difficulty in many cases, and frequently cannot be established sooner than the middle or end of the second week of the attack. We cannot depend upon the character of the pyrexia alone, for this is often more decidedly remittent in cases presenting the anatomical lesions of enteric fever, than in others in which they are absent and which have been diagnosed as remittent fever[2] by competent observers; and the pathognomonic symptoms of typhoid are not developed until the second week of the disease. Moreover, the rose-colored eruption of enteric fever is not always to be found in undoubted cases. Under these circumstances we must do the best we can, and will often be obliged to reserve our diagnosis until by the successful application of the quinine test we are able to demonstrate that the disease is malarial, or by its failure and the appearance of the pathognomonic symptoms of enteric fever we ascertain that the typhoid element is the controlling one in the evolution of the febrile and other phenomena which characterize the case. We will be greatly aided, however, in making an early diagnosis, by the previous history of the patient. If he has been subject to repeated attacks of intermittent fever, and has recently been exposed to malarial influences, we may give precedence to the theory that his present attack is of malarial origin; and, in this case, the "quinine test" should be applied at once in an efficient manner. Its failure when not properly applied is illustrated by the case we have copied from Sir Joseph Fayrer's recent work (page 236). Small doses are thrown away on these individuals, as they have acquired a certain tolerance to the physiological effects of the drug, from having frequently resorted to it for the cure of attacks of "ague." It will, therefore, be necessary to give it in full doses in order to test its power to arrest the progress of the disease. If it prove that, notwithstanding the malarial history of the patient, the attack is one of enteric fever, the physician will have done no harm in commencing the treatment of this disease in a malarial subject by a few *full* doses of the great anti-malarial remedy. Small doses, however, often have the effect of increasing headache and febrile excitement in this disease. When, on the other hand, there is no history of previous intermittent attacks or of recent exposure to malaria, and especially when a patient, previously healthy, falls sick with a fever of a mild grade at first, but in which there is a daily increase in the degree of pyrexia and an absence of those symptoms which commonly attend first attacks of remittent fever—severe headache, bilious vomiting, etc.—the presumption is altogether in favor of the view that the case is one of typhoid fever, and expectant treatment may be adopted.

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[1] Op. cit., p. 270.

[2] See Charts Nos. 18 and 19, with accompanying clinical histories and post-mortem notes, page 262.

The differential diagnosis between adynamic remittent fever and yellow fever is also, in many cases, attended with great difficulty. This is shown by the fact that mistakes in diagnosis are constantly made by experienced practitioners when yellow fever makes its appearance unexpectedly in localities outside of its endemic prevalence. The first cases are so often pronounced "malignant malarial fever," or "pernicious remittent fever," or simply "remittent fever," or "malarial fever," that it may almost be said to be the rule rather than the exception that this mistake is made. Solitary cases also occasionally occur in our Southern seaport cities, in regard to which physicians of equal experience differ, as regards diagnosis, when they have not only the whole clinical history, but the post-mortem appearances to guide them. Nevertheless the clinical features of the two diseases are, in well-marked cases, sufficiently distinct, and the differential diagnosis may be established more promptly and with less difficulty than when the question is between typhoid and remittent fevers. The continuous course of the febrile movement in a typical case of yellow fever; the gradual defervescence by a single descending curve from the acme of pyrexia, which commonly is reached within the first twenty-four hours; the notable depression of the vital powers during the stage of calm, while the mind remains clear and the patient is unconscious of the perils attending his situation; the presence of albumen in the urine; and in fatal cases suppression of urine and black vomit, are all distinguishing features of this disease. On the other hand, in adynamic remittent fever the remittent character is sufficiently distinct at the outset of the attack, and instead of a gradual decline to a temperature approaching the normal—and sometimes sub-normal—the febrile exacerbations reach a higher point as the case progresses. The partial remissions are in no way comparable with the stage of calm, so characteristic of yellow fever, and the urine is almost invariably free from albumen; while, in contrast with the usually clear intellect of yellow fever, delirium is very apt to be present.

It is true that severe cases of yellow fever, after a brief calm stage, are attended with a reactionary fever which sometimes assumes a typhoid character, and in which the symptoms are nearly identical with those which Professor Maclean has described as characterizing the "adynamic remittent fever" which he encountered in India. As already stated, we suspect that these cases were in truth cases of septic poisoning resulting from exposure to the decomposing filth of a large tropical city, rather than cases in which malaria was the leading etiological factor. Without doubt similar cases occasionally occur in our own large Southern cities, and it is not improbable that many of the "sporadic" cases of yellow fever which have been reported are of this character.

Prognosis.—A large proportion of the reported mortality from remittent fever, especially in tropical regions where this title is made to include a multitude of cases not strictly malarial in their origin, is due to the fatal character of the adynamic form of the disease. The victims are, for the most part, individuals who prior to the fatal attack were in a cachectic condition as a result of protracted exposure to malaria, to septic influences —filth—to depressing climatic conditions, or who from intemperance, improper food, etc., are in a condition of reduced vital resistance. In many of these cases, also, there has been more or less damage to the excretory organs by the continued action of the causes mentioned, and the adynamic symptoms in a certain proportion of the cases are probably due to the defective elimination of poisonous products formed in excess during the febrile paroxysm.

The following quotations from the recent work of Sir Joseph Fayrer show the enormous mortality in India from "fever," attributed in a general way to malaria,[1] and the marked influence upon the death-rate of that most potent factor, scarcity of food, to which the adynamic character of malarial fevers is frequently due in that populous country:

> Let us now speak of the extent to which fever prevails, and some of the reasons why it does so. Official records afford proof that it causes an amount of sickness and mortality that is hardly credible, and in some years almost challenges comparison with the black death which ravaged Europe in the fourteenth century and destroyed a fourth part of the whole population. The registered deaths from all causes in India in the year 1879 were 4,975,042: cholera accounting for 270,552; small-pox accounting for 194,708; bowel complaints accounting for 250,173; fevers accounting for (out of a population of 187,105,833) 3,564,035.
>
> Let us look at the statistics of fever prevalence as illustrated by the sanitary reports and returns of hospitals in Calcutta.

The records of six of the principal Calcutta hospitals show that the number of cases diagnosed as "remittent fever" greatly exceeded the number recorded under the heading "typhoid or enteric fever," being in 1880, 926 of the former to 8 of the latter. Professor McConnell, who obtained the statistics for Fayrer, remarks: "A comparison of these tables is very interesting, as showing the relative frequency of typhoid and remittent fever in various years, *these being the two kinds of fever often so difficult during life to differentiate.*"[2]

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[1] In the present state of registration it is not possible to define the special character and type of these fevers. They are certainly for the most part malarial in character (op. cit., p. 14).

[2] Italicised by present writer.

> The Sanitary Commissioner's Report for 1879 shows that the general causes which influenced the public health in fever localities were undrained ground into which canal-water had been led, and rainfall added to the already waterlogged soil. In 1880 food became cheaper, and except in certain districts there was less rain. *In* 1879, *during the great scarcity of food, the fever death-rate was* 37.82 *per* 1,000; in 1880 it fell, with increase of food, to 23.11 per 1,000, which was still above the five years' average of 20.91 per 1,000. . . .
>
> The total annual deaths from fever taken through the scarcity period were:
>
> | | | | |
> |---|---|---|---|
> | 1877 | 574,722 | 1879 | 1,616,108 |
> | 1878 | 982,117 | 1880 | 987,220 |
>
> The fundamental cause of the great loss of life from fever was increased predisposition from scarcity of food.

No doubt that portion of mortality represented by the above figures which properly comes under the heading "malarial remittent fever" was due in great part to cases of adynamic type. We may say, then, that adynamic remittent fever is an exceedingly fatal disease, but the prognosis in any particular case must be governed by its individual history and by the nature of the predisposing cause or complication to which the adynamic tendency is due.

MORBID ANATOMY.—The pathological lesions in adynamic remittent fever, when this is truly malarial, do not differ from those found in other fatal forms of malarial fever—pernicious or congestive intermittents or remittents. But in addition to these—pigmentation, enlarged spleen, etc.—there is frequently evidence of secondary intestinal or cerebral complications, and of pre-existing visceral disease of a chronic nature. The reader is referred to the article on "Pernicious Intermittent Fever" for an account of the lesions peculiar to malarial diseases, and to the post-mortem notes relating to the appended cases for those found in "adynamic remittent fever."

SYMPTOMS.—The symptoms of adynamic remittent fever have already been given in our discussion of questions relating to etiology and diagnosis. They are those which characterize the "typhoid state," and are summarized by Professor Wood as follows:

> Connected with more or fewer of the characteristic symptoms of bilious fever, before enumerated, are, at a comparatively early period of the disease, a dark and dryish tongue, with sordes about the gums and teeth; dark alvine evacuations, becoming in the end involuntary; flatulent distention of the abdomen; irregularity of respiration; a pulse either frequent or slow, slender or full, regular or irregular, but always feeble and readily compressible, and sometimes almost fluttering; a strong tendency to passive hemorrhage, as shown by oozing of blood from the gums, discharges of dark blood from the bowels, petechiæ and vibices upon the skin; a dusky, livid, or purplish hue of the surface, often combined with the yellow of bilious disease; irregular distribution of heat over the body; and the early occurrence of low delirium, stupor, or coma, or in their absence of great restlessness, jactitation, anxiety, and mental depression.[1]

These symptoms correspond with those given by Maclean as coming under his observation in cases admitted during the autumn months into the Residency hospital, "from the malarial quarters of that densely populated and most unsanitary city," Hyderabad in the Deccan.

In Rome also the same symptoms were observed by Colin in cases denominated by him *fièvre subcontinue estivale*, to distinguish them from the *subcontinue automnale*, which is said to differ from the first-named form in that it occurs most frequently in cachectic individuals suffering from intermittent fever of a prolonged type—tertian or quartan—and in running a protracted course.[1] The summer form, on the contrary, is developed during the season of greatest heat in the course of simple remittent fever, and is remarkable for the intensity of the febrile phenomena and the rapidity with which the patient falls into the typhoid condition.[2]

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[1] Op. cit., vol. i., p. 285.

Morehead also has occasionally encountered cases of the "malignant form" of remittent fever in the general hospital at Bombay, and says:

> When these phenomena of depressed vital action are present in their most aggravated degree, petechial spots may show themselves on the surface of the body, or there may be oozing of blood about the gums and lips, or epistaxis, or vomiting of blood or of dark-colored grumous-looking fluid; or mælæna or hæmaturia may be present.

These hemorrhagic cases were, however, extremely rare; but cases of ordinary remittent tending to become continued and then adynamic in character were not infrequently observed, both among the native and European population. The following instructive account of the clinical history of these cases is given:

> It has been stated that sometimes in ordinary remittent fever the exacerbations are double—one in the day, another in the night. Such cases are generally severe, because the hours of exacerbation are increased in number; and it often happens that after the first or second day of the double exacerbation, or it may be from the very commencement of the attack, the remissions are so slight as to be hardly observed: the fever becomes almost continued in character. This may proceed from the intensity of the malaria acting on an ordinary constitution, or from a less degree of malaria acting on an asthenic constitution, or (and this is probably a very frequent cause) from the early exacerbations not having been judiciously managed—from neglect of the withdrawal of causes of irritation or excitement, or by means of cure too depressant. Finally, the continued form may be favored by the access of local inflammation.
>
> When remittent fevers which have thus passed into the almost continued form do not prove fatal in the early stages from sudden depression of the vital actions of the nervous system or of the heart, or from congestion, or inflammation of some important organ, but continue beyond the eighth day, or earlier when the asthenia has been great, then a new train of symptoms begins to appear. The pulse becomes more frequent and feeble, the tongue dry, brown, and unsteadily protruded. The hands tremulous, with tendency to subsultus tendinum. There is more or less muttering delirium, and death takes place from exhaustion or coma. In other words, the remittent fever has assumed an adynamic character.[3]

TREATMENT.—As adynamic symptoms result, in some instances at least, from the intensity and duration of the febrile movement and the blood and tissue changes connected with it, our first object should be to moderate the intensity of the pyrexia and arrest its course as promptly as possible by specific treatment. When a well-directed effort fails in accomplishing this it will commonly be owing to the fact that although remittent in type the fever is not malarial in its origin, or at least that the malarial element if present is not the controlling factor in the evolution of the morbid phenomena; or it will be due to some complication, pre-existing and of a chronic character, or secondary and of an inflammatory nature—*e. g.*, cerebral, gastro-intestinal, hepatic. In the former case we have nothing to do but to accept the situation, and if we do not change our diagnosis should at least adopt the treatment suitable for a continued—protracted and self-limited—fever.

No doubt the specific and antipyretic treatment recommended is also the best preventive treatment so far as complications of an inflammatory nature are concerned; but when inflammation has occurred, the propriety of continuing the specific treatment is questionable. It is probably in these cases mainly that quinine has been observed to do harm, and it will be necessary to administer it cautiously, if at all. We must especially be careful that the local hyperæmia of the gastro-intestinal mucous membrane and of the viscera generally, which results from the paralyzing action of the malarial poison, does not pass into inflammation as a result of injudicious treatment. The indication is evidently to relieve the vaso-motor paralysis and thus permit the engorged capillaries to empty themselves, and not to apply the spur of local stimulants. A congested liver or hyperæmic gastro-intestinal mucous membrane can no more be whipped into functional activity without danger than can a congested brain. Every one understands that in the latter case complete functional inactivity—rest—and nervous sedatives—especially ice—are useful, and that cerebral stimulants are dangerous. But the same principle of treatment is not so universally recognized as applicable to other organs in a similar condition. We have the high authority of Morehead for the statement that "too much general blood-letting, leeching, antimony, calomel, catharsis, and the neglect of quinine and nourishment" may give rise to the development of adynamic symptoms. In this country we believe that general blood-letting, leeching, and antimony may be stricken from the list as common causes of the development of a typhoid condition, and American physicians generally fully appreciate the value of quinine and nourishment. But is it not true that calomel and catharsis occupy too prominent a place in the treatment of remittent fever in some parts of the country? In asking the question it is not our intention to deny *in toto* the value of mercurials and the necessity of resorting to the use of cathartics in the treatment of remittent fever; but we do not hesitate to join Dr. Morehead in protesting against the disastrous course of attempting to *cure* this disease by purging, or by bringing the patient "under the influence of mercury." Non-irritating cathartics will be required from time to time for the removal of irritating material from the *primæ viæ*. And it may be that calomel is especially useful in consequence of its *antiseptic* properties. Certainly it often has a very happy effect in altering the character of the discharges when they are of an offensive and septic character. It is extremely probable that one of the causes of the "typhoid state" is the absorption of septic poisons formed in the bowels as a result of the putrefactive decomposition of ingested material and of the intestinal secretions. In a state of health the normal secretions prevent these putrefactive fermentations, but when the mucous membrane and the glands are in an intensely hyperæmic condition there is no secretion, or it is of a different nature, and under the influence of a high temperature the changes referred to occur very promptly. Under these circumstances we have meteorism and the intensely offensive discharges which characterize this condition. If it be true, as we suspect, that whatever benefit is derived from the administration of calomel is due to its antiseptic action upon the contents of the bowels, rather than to any power to alter favorably the secretions of the intestinal mucous membrane, then it is worth while to inquire whether some more harmless antiseptic may not be substituted for it. Recent experiments show that, instead of being a cholagogue, calomel diminishes the secretion of bile, and its use as an antiphlogistic remedy to control inflammation has now been generally abandoned. Yet it is conceded by experienced practitioners that it may often be administered with advantage in gastro-intestinal disorders resulting from the presence of fermenting material in the alimentary canal, and it is very extensively prescribed as an "alterative" in remittent fever.

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[1] See clinical history of case on p. 263.

[2] See cases and remarks, p. 262.

[3] Op. cit., p. 62.

Although no doubt frequently useful, and probably in the way we have suggested, it must be remembered that calomel is something more than a germicide and antiseptic, and that its constitutional effects are especially dangerous in diseases having an adynamic tendency.

When a remittent fever does not yield to specific medication, and adynamic symptoms are developed in spite of our efforts to keep the temperature within bounds by antipyretic treatment, we can only persist in these efforts, and in addition devote ourselves to supporting the strength of the patient by the systematic administration of nourishing food and of stimulants. In short, the treatment will not differ from that of typhoid fever, unless local complications call for some special attention.

Liquid nourishment will be required, as the stomach is not in a condition to digest solid food. The main reliance must be upon milk and animal broths, which should be given at regular intervals—about every two hours—alternately with a proper amount of good wine or whiskey.

Dr. Manson speaks very highly of turpentine, which was Professor Wood's favorite remedy for typhoid fever. This, he says, "may almost be regarded as a specific" in adynamic remittent fever.

> It is more suitable than quinine in this condition, as it is better tolerated, and while it possesses febrifuge properties very similar to the alkaloid, it also exerts a happy influence over the gastric and intestinal irritation so commonly present. It may be given in doses of ten to twenty drops in emulsion, repeated every three or four hours until the symptoms yield. It should be persisted in until the patient is fairly under its influence, unless the effects it occasionally produces, viz., hæmaturia, strangury, or its peculiar intoxication, supervene, when, of course, it should be discontinued.[1]

CASES.—The following cases are from Fayrer's recent work. It will be noticed that the character of the pyrexia is more decidedly remittent in the second case diagnosed "enteric fever" than in the first called "remittent:"

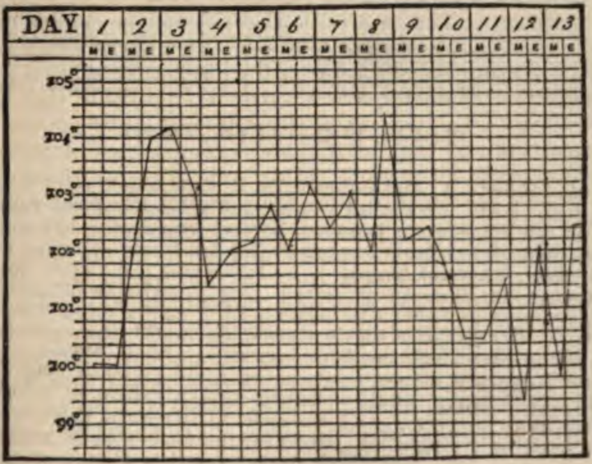

Chart No. 18 (Case XVII., Fayrer).

CASE XVII.—*Remittent.*—R——, a Hindu, aged twenty years. Admitted October 21, 1880. Has been suffering from fever of apparently a remittent type for the last eleven days, and during this period the bowels have also been very loose. Body moderately well nourished; conjunctivæ injected; tongue moist at the edges and coated and dry at the centre. Complains of pain on pressure over the right hypochondriac region. The spleen is slightly enlarged. Has a troublesome cough, and on auscultation moist râles with wheezing and cooing, etc., are heard in the interscapular space and at the bases of both lungs posteriorly. Pulse full and quick. Skin hot but moist; temperature, 100°.

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[1] Virginia Med. Monthly, Oct., 1881, p. 520.

October 22d.—Patient restless and inclined to be delirious Stools frequent and highly bilious. Cough troublesome, and the expectoration is scanty, frothy, and tenacious.

October 23d to 27th.—Becoming quite delirious on the 23d, the patient remained so more or less continuously. The cough, looseness of the bowels, etc., persisted in spite of treatment. Occasional twitching of the limbs and subsultus were noticed. The tongue dry, and sordes over the gums and teeth.

October 28th to November 2d.—No improvement; very restless and delirious. Is fed with difficulty. Stools less frequent but passed unconsciously. High temperature persistent. The patient gradually became weaker, and died exhausted and semi-comatose, the pupils dilating some hours before death.

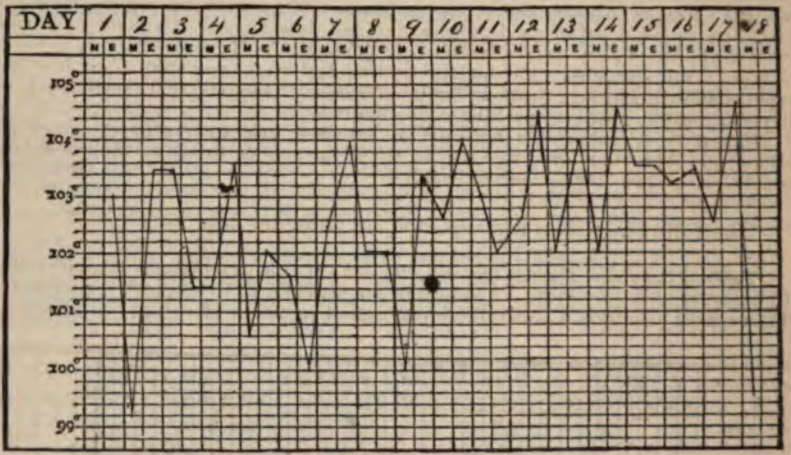

Chart No. 19 (Case LXVII., Fayrer).

Treatment.—At first: ℞. Vini antimonialis, ♏ x.; tr. cinch. co., ʒ j.; decoct. cinch., ℥ j.; every three hours. Ice applied to head and a sinapism to the back of the chest. Afterward, as the temperature persisted, several hypodermic injections of neutral quinine were given, but seemed to produce but temporary defervescence. ℞. Mist. liq. ammon. acet., ℥ j.; vini ipecac, ♏ x; tr. aconiti, ♏ ij.; every three hours for more than twenty-four hours was also given. Lastly, carbonate of ammonia and bark.

Post-mortem fourteen hours after death.—Rigor mortis strong. Body moderately well nourished. The sinuses of the dura mater are loaded with dark fluid blood, and the vessels of the pia mater throughout intensely engorged. There is a good deal of serous effusion into the meshes of this membrane, but no actual inflammatory exudation (lymph). Each lateral ventricle contains about a drachm of sanguineous serum. The brain substance is everywhere hyperæmic, but otherwise presents nothing abnormal. *Heart* moderately contracted. Right cavities filled with dark fluid blood. The left auricle contains a little fluid blood, the left ventricle a small slightly decolorized clot. *Valves*, etc., healthy. Both lungs are large, heavy, of an intense dark purplish color, and loaded with frothy sanguineous serum. The bases semi-solid, soft, and œdematous (hypostatic pneumonia). *Liver:* Large, smooth, substance very dark and soft. Bile-ducts prominent and full. Gall-bladder about half full. Bile thin, reddish-yellow, measures about three drachms; weight of liver three pounds four ounces. *Spleen:* Enlarged, capsule thick and opaque; substance soft, pulpy, very dark; weighs fifteen ounces. *Kidneys:* Heavy and juicy from recent venous congestion; nothing else remarkable. Mucous membrane of stomach pale and anæmic. That of the whole of the small intestine slightly hyperæmic, particularly in the ileum. There is no affection, however, of the glandular structures. In the cæcum and ascending colon there are patches of recent vascularity; the rest of the large gut healthy. The mesenteric glands are a little swollen and hyperæmic. The stomach contains four ounces of greenish-yellow fluid—almost pure bile—and the small intestine half an ounce of soft, brownish feculent matter. The large gut contains two ounces of semi-solid fæces.

CASE LXVII.—*Enteric Fever* (under the care of Dr. Joubert, General Hospital, Calcutta).—W. M'C——, aged twenty-four years, seaman, Scotch; five weeks in India; admitted July 27, 1878; died August 15th. Suffered from fever, coming on at night, for two days before admission. Great headache; tongue coated; skin moist; bowels not open. No particular symptoms at first beyond pains in head and limbs; hot, dry skin; thirst; irregular bowels till August 1st, when there was free perspiration and loose bowels. 2d, same febrile symptoms, with griping pain in bowels and pain on pressure over colon. 4th, looseness of bowels and abdominal pain; other symptoms unchanged. 6th, great tenderness on pressure all over the abdomen; bowels loose; tongue furred and fissured; some delirium; skin hot and dry; tremor of muscles. 8th, abdominal pain and tympanites; pupils dilated; herpetic eruption on chest; no motions. 10th, conditions unchanged; pupils dilated; tremulous tongue; constipated. 11th, drowsiness, delirium, and unconsciousness; bowels open; frequent micturition; great weakness; tongue furred, yellow. 12th, conditions the same; motion in the bed-clothes. 13th, comatose; hiccough; vomiting and great emaciation; pupils dilated; rapid shallow breathing; death at 4 P.M. *Treatment:* salicylic acid febrifuge, quinine hypodermically, wet-sheet packing, and stimulants.

Extract from Post-mortem Notes.—Very extensive ulceration of Peyer's patches and solitary glands in the lower two feet of the ileum; no perforation. Spleen enlarged, weight one pound. Other organs healthy.

The following cases are reported by Guéguen (op. cit.):

Typhoid Remittent Fever (Chart No. 20).—A——, private Second Regiment Marine Infantry, aged twenty years. Taken sick August 30th, at 4 P.M., with moderate fever. The typhoid condition was not developed until September 3d.

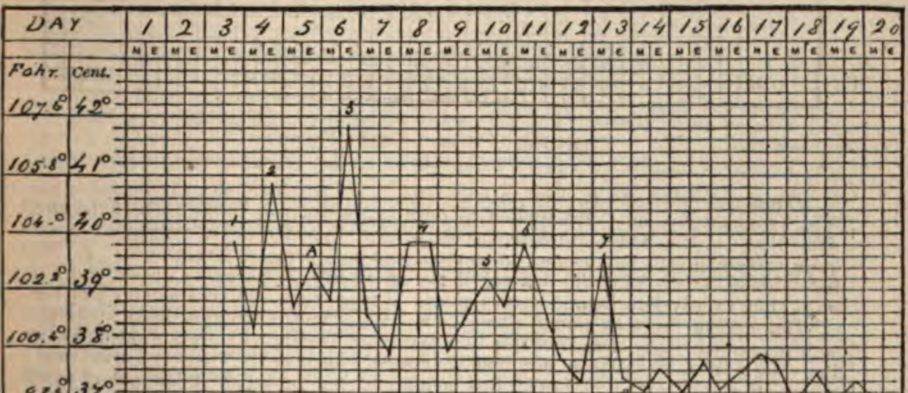

Chart No. 20 (Guéguen).

1, 2, 3 (the figures refer to the chart). Intense fever with remission each morning. Epistaxis, dizziness, gurgling in the right iliac fossa; countenance stupid, face flushed.

A. Antispasmodics, purgative enema, quinine.

4, 5, 6, 7. Potion of bromide of potassium. Continued somnolence, less during the remissions. Icteric tint of the conjunctivæ and integument; bilious vomiting (once); abdomen very painful on pressure, inflated. Sudamina.

8. The symptoms improve and convalescence is established. Defervescence on the thirteenth day.

Typhoid Remittent Fever (Chart No. 21).—C——, private Second Regiment Marine Infantry, aged twenty-three years. Has been sick two days. Cephalalgia, dizziness, ringing in the ears ; countenance stupid.

1. Purgative enema (the figures refer to the chart).
2. Somnolence ; twenty leeches applied to mastoid processes.
3. Same condition but less fever. Sulphate of quinine, 2 grm. (about 30 gr.) in three doses. Purgative enema. Vomiting.
4. Amelioration in the symptoms. Sulphate of quinine, 1 grm. (15 gr.).

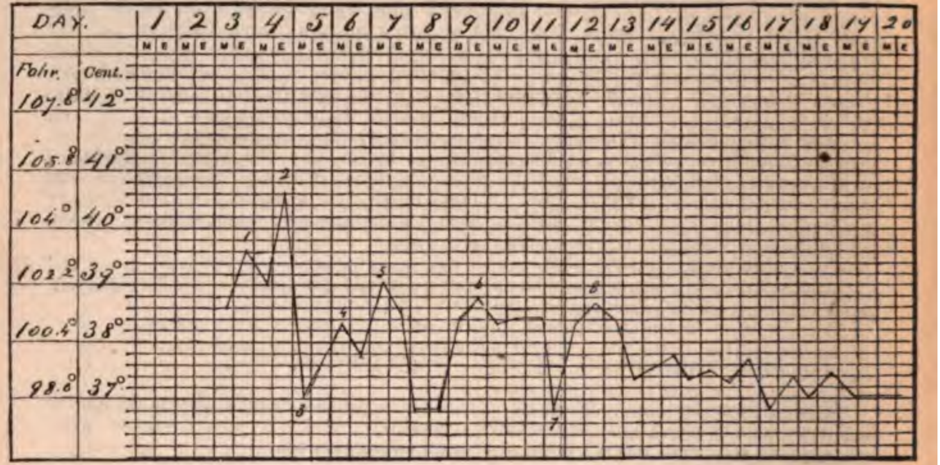

Chart No. 21 (Guéguen).

5. Fever ; delirious during the night, no sleep, great agitation. Potion containing 6 grm. of bromide of potassium in 45 grm. of spirits of morphia.
6. Same condition ; dark stains upon the thorax.
7. Notable improvement, but adynamic. Potion containing 50 grm. of rum. Alimentation.
8. This last exacerbation was not accompanied by any alarming symptoms, and was followed by convalescence.

Remarks.—This case was characterized by the absence of any inflammatory phenomena ; adynamia appeared early ; tranquil delirium from sixth to tenth day.

The following cases are reported by Colin (op. cit.) :

Fièvre Subcontinue Typhoïde—Death in the Algid Condition—Gangrenous Condition of Peyer's Patches.—L——, *voltigeur* Fifty-ninth Infantry. In Italy a year and a half ; aged twenty-eight years; has been in hospital four times with intermittent fever ; stationed in the quarter *Ponte Rotto.* Admitted to hospital—Sainte-Thérèse—August 31, 1865. The previous evening he was suddenly seized with pain in the head and loins ; face red, cheeks purple ; pulse 110, full and hard. The patient still cries out with the headache ; the tongue is yellow ; continual nausea ; constipation. Abdominal palpation shows that the spleen is considerably enlarged. *Prescription :* Potion containing 2 grm. of ipecac ; at three o'clock, when vomiting had ceased, the patient took in our presence 15 degr. (about 23 gr.) of sulphate of quinine.

September 1st.—Marked diminution of the fever, headache, and nausea. *Prescription :* fifteen degr. of sulphate of quinine ; purgative enema.

September 2d.—Epistaxis during the night, and great agitation ; face stupid ; lips tremulous ; tongue dry ; pulse "undulating," almost dicrotic. *Prescription :* Sulphate of quinine, 1 grm.

September 3d.—Nocturnal delirium alternating with agitated dreams, during which the patient constantly attempted to get out of bed ; epistaxis ; slight meteorism ; bowels not moved since evening of September 1st. *Prescription:* Potion containing 1 decgr. of musk; purgative enema.

September 4th.—Subdelirium at time of visit. The typhoid symptoms continued during the following days, without being aggravated, and we believed the patient to be improving, when on the 9th, at our evening visit, we found a considerable reduction in the temperature and a feeble pulse and voice; and notwithstanding the most energetic employment of stimulants, the algidity augmented and the patient died at 10 P.M.

Autopsy, September 10th.—*Head:* We found nothing but congestion of the subarachnoidean vascular net-work, without effusion or alteration of the brain substance. *Heart:* Yellowish, very soft, distended by soft dark-colored clots; lungs healthy. *Spleen:* Very large, weighing 1,040 grm.; softened throughout, but more especially at the centre, where the pulp presents in places a color almost black, owing to the great quantity of pigment granules. *Liver:* Also hypertrophied (about 2,000 grm.), of a uniform mahogany color. *Intestine:* All of Peyer's patches are enormously tumefied, and project, at certain points, 5 or 6 mm. above the level of the mucous membrane. Near the ileo-cæcal valve there are numerous ulcerated *plaques*, having abrupt margins and pulpy, grayish surfaces. The mesenteric glands are hypertrophied.

Fièvre Subcontinue Typhoide—Tetanic Symptoms—No Intestinal Lesion.—B——, private Nineteenth Infantry, aged twenty-two years; in Italy eleven months; stationed in the quarter of *Salara* (the most dangerous, perhaps, in Rome). Admitted to hospital—Saint-André—August 3, 1864. Attacked with symptoms of remittent fever of moderate intensity; headache, flushed face, hot skin, coated tongue, intense thirst, agitation, and vomiting. *Prescription:* Two grm. of powdered ipecac; 1 grm. of sulphate of quinine, to be taken at three o'clock

August 4th.—The same symptoms persist; considerable nocturnal agitation; epistaxis at time of visit. *Prescription:* Seidlitz water; 6 decgr. of sulphate of quinine.

August 5th.—Epistaxis repeated; pulse dicrotic; tongue dry; diarrhœa; slight meteorism. During the following days the fever and diarrhœa continued, and meteorism increased; delirium became constant. On the 9th we discovered sibilant râles, disseminated, on both sides of the chest.

August 12th.—Eruption of sudamina, almost confluent; subsultus tendinum; irregular pulse; involuntary discharges from bowels.

August 14th.—The patient seemed a little better at the morning visit, and was able to reply to questions; but during the following night he was seized with convulsive movements, and the following day (August 15th), at our morning visit, we found him with his head thrown back, lips and face purple, thorax protruding and immobile, and already nearly asphyxiated by tetanic contraction of the muscles of the thorax. Notwithstanding the immediate resort to chloroform by inhalation and of revulsants to the extremities and thorax, he died at 10 A.M.

Autopsy, August 16th—Congestion of the subarachnoidean vessels without trace of serous or bloody infiltration of the pia mater or adherence of this membrane to the cerebral substance. *Lungs:* Much distended, protruding from the opening made in the chest-walls; no organic alteration; frothy mucus in all the bronchial ramifications. *Heart:* Slightly yellowish in color and presenting a purple ecchymosis under the pericardium—three centimetres long and ten to twelve millimetres broad—along the anterior furrow; right cavities distended. Congestion of the mesenteric veins, but only in their principal branches; the *small intestine* is of a pale color, which contrasts strongly with the purplish-red color of the stomach. *There is no alteration in color, volume, or consistence of Peyer's glands*, and not the slightest swelling of the mesenteric glands. The *spleen* is three times the normal size, extremely soft, and presents blackish patches where its tissue is most diffluent. Upon microscopic examination these prove to contain an immense quantity of pigment granules of all forms. *Liver:* Slightly marbled, normal in volume and structure.

Fièvre Subcontinue Automnale—Petechiæ—Parotiditis—Recovery.—B——, private Fifty-ninth Infantry; in Italy two years; previously admitted to hospital three times for intermittent fever. Is yellow, emaciated, and has œdema of lower extremities. Was ordered to be returned to France (August 25, 1866), but upon arriving at Civita Vecchia, where he was to embark, was seized with a violent chill attended with faintness and vomiting. His condition appeared to me so grave that he was at once transported to the military hospital of which I was surgeon-in-chief.

The following day (August 26th) he was found to have a pulse of 120, hot skin, flushed cheeks; no pulmonary complication. Was delirious during the night and passed urine involuntarily. *Prescription:* One grm. of sulphate of quinine; coffee, bouillon.

August 27th.—Tongue black, fissured; epistaxis, meteorism without diarrhœa; subsultus tendinum; pulse 116. This condition continued without notable modification until September 2d, when, at the time of our evening visit, the patient had a violent chill, of which he seemed conscious notwithstanding his profound stupor. *Prescription:* Opiate enema, with 2 grm. of sulphate of quinine; potion containing musk (5 ctgrm.).

September 3d.—Coma since yesterday evening; sensibility preserved; trismus. *Prescription:* Fifteen degr. of sulphate of quinine by enema

September 4th.—Notable improvement; intelligence has returned; tongue still dry and blackish; pulse has fallen to 90. The controlling symptom is profound adynamia with general muscular trembling. (Soup, wine, coffee, decoction of quinquina.)

September 8th.—During the night the patient was again taken with a chill and vomiting; stupor returned, with involuntary micturition; tongue fissured and fuliginous; considerable tumefaction in the hypochondria and development of splenic dulness. Skin hot, pulse 110. *Prescription:* One grm. of sulphate of quinine; potion containing ether, ice.

From this time until about September 25th the adynamic symptoms continued to increase; a discrete, purple, petechial eruption appeared upon the flanks and thighs, and an erysipelatous blush over the sacrum. Continuous mild delirium; the pulse and temperature presented irregular oscillations; general bronchitis with congestion at the base of right lung.

September 25th.—The right parotid, which the previous evening seemed a little tumefied, became enormously enlarged, and the cellular tissue of the neck œdematous.

September 27th.—The parotid abscess was incised. After September 30th the patient, who had reached an extreme degree of debility, seemed to undergo a complete transformation; the appetite and natural sleep reappeared; the parotid wound and excoriation of the sacrum healed rapidly; but it was not until October 25th, two months after his admission to hospital, that the patient was able to sit up. He was then very yellow, dropsical, and subject to nervous trembling. In this condition we sent him to France November 12th.

Remarks by M. Colin:

We see how many grave accidents have menaced this patient, from pernicious phenomena, coma in particular, to the most serious complications of malignant fevers—petechiæ, gangrene, suppuration of the parotid. It is to fevers of this kind that M. Haspel has given the name *fièvre putride scorbutique*, an appellation which indicates perfectly the hemorrhagic and gangrenous tendency of the affection. All of those attacked in this way were old cases, often in hospital for a long time; in all the affection arrived late in the season, when cachexia was at its maximum; in nearly all, to coma, algidity, epistaxis, was joined gangrene of the cheek, of the gums, of the tongue, of the genital organs, of blistered surfaces. In our opinion all of these cases were grave forms of the subcontinued autumnal fever.

Pernicious Remittent Fever.

Definition.—Those cases of remittent fever are denominated *pernicious* in which symptoms threatening life are developed as a result of defective innervation, due to the paralyzing action of the malarial poison. The pernicious character is manifested by great feebleness of the heart's action and the development of the *algid* condition, or by dangerous visceral congestion, and especially of the brain—*comatose* form.

Synonyms.—Pernicious fever; grave remittent fever; congestive fever.

We do not include under this heading those forms of malarial disease which owe their fatal character to blood changes directly or indirectly due to malaria—destruction of red corpuscles or formation of secondary products of a poisonous nature; or to complications—jaundice, dysentery, inflammation of various organs etc.; or to cachexia due to chronic malarial poisoning, scorbutus, inanition, etc.; or to passive hemorrhages, which are liable to occur in scorbutic subjects and in the victims of chronic malarial poisoning.

These various predispositions and complications often give a malignant character to individual cases or to groups of cases subjected to the same influences, and the term "pernicious" is not infrequently applied to cases of this kind. But most recent authorities agree in restricting the use of this term to such cases as come within the limits of our definition. Colin, however, includes under the heading "*Fièvre pernicieuses solitaires*" the forms of malarial disease described by him as *fièvre subcontinue estivale* and *fièvre subcontinue automnale*, which we have included in our account of "Adynamic Remittent Fever."

Etiology.—The pernicious phenomena developed in the course of a remittent fever do not differ from those already described under the heading "Pernicious Intermittent Fever," and, as already stated, the dividing line between these two forms of malarial disease is not well defined, and indeed is quite artificial. But remittent fever is recognized as a graver form of malarial poisoning, and as commonly due to recent exposure to malaria. It is, accordingly, in this form of the disease that we should expect most frequently to encounter pernicious symptoms. And such is in truth the case. Pernicious remittent fever is especially common in intensely malarial regions, and is attended with greater danger to life than pernicious intermittent.

Inasmuch as the pernicious symptoms are due to the paralyzing action of the poison upon the nervous system, it is evident that the result depends upon two factors: the potency of the paralyzing agent and the resisting power of the nervous elements involved. The second factor is largely influenced by the previous history of the individual. One person, for example, may have an enfeebled brain as a result of previous disease, habits of intemperance, etc.; in another the sympathetic nervous system may be especially susceptible from recent or remote depressing causes, or from an inherited predisposition.

When pernicious symptoms are developed in the course of an intermittent fever due to exposure at a remote date, we may infer that they are a result of diminished resisting power, and this is often no doubt in consequence of repeated attacks of ague. When, on the other hand, pernicious phenomena attend a first attack in a previously healthy person, it is commonly owing to recent exposure to malaria in an intense form.

This is a comparatively rare event outside of the tropics. Even in the vicinity of Rome it is said by Colin to be an infrequent occurrence, at least in the localities occupied by the French troops. But during the most dangerous season, exposure at night in crossing the Pontine marshes occasionally causes an attack in which pernicious symptoms are developed at once—d'emblée—in an individual previously healthy. Previous attacks of intermittent or remittent fever are considered by the author mentioned the most potent of the predisposing causes to pernicious complications. This is doubtless true so far as the algid form of pernicious fever is concerned, but it is not equally true of the comatose variety, which frequently attacks by preference individuals of sanguine temperament who have not previously suffered from malarial disease. Those cases of this form in which the patient is first seen in a comatose condition which has been developed suddenly, are frequently due to the influence of a second factor.

Most frequently the second factor is an elevated external temperature, and this especially is the case of unacclimated strangers in tropical regions. Evidently if the attack is due to exposure to heat alone, the case is not one of pernicious remittent, but of "thermic fever," and doubtless many cases of this kind have been improperly ascribed to the action of malaria.

The combined effects of malaria and alcohol may also give rise to cerebral congestion and coma, and not infrequently the pernicious character of an attack in those cases in which the patient is found in a comatose condition, is due to the combined influence of these two paralyzing agents.

Diagnosis.—When pernicious symptoms are developed in the course of a simple remittent fever the diagnosis will present no difficulty. But when the immediate cause of the attack is alcoholism or insolation, it will often be difficult to decide at first what share malaria has in producing the cerebral congestion and coma. Fortunately the immediate treatment is the same in either case, and if coma is not promptly relieved by the cold douche or an ice-cap applied to the head and revulsive remedies, we need not hesitate to give quinine by enema or by hypodermic injection, for this is good treatment in insolation as well as in malarial coma. If malaria is, in truth, the controlling factor in the case, this will be shown later by the remittent character of the fever and by the tendency to a return of the pernicious symptoms at intervals of twenty-four or forty-eight hours. During the epidemic prevalence of cholera, or in regions where it is endemic, the algid condition developed in this disease might easily be mistaken for that resulting from the intense action of the malarial poison. Indeed, it has been claimed by English physicians in India that both forms of disease are produced by the same poison—malaria. It is hardly necessary to say that this view is entirely untenable, inasmuch as malaria in a sufficiently intense form to produce algid phenomena does not in the United States give rise to choleraic symptoms. Still there is, as remarked by Morehead, considerable analogy between the symptoms of this form of fever and those of cholera.

> The collapse of cholera resembles in many features the stage of congestion, and when secondary fever occurs it is not unlike the reaction which sometimes attends the congestive form of remittent fever. The secondary fever of cholera is, however, apt to run a longer course, and to be complicated with subacute inflammation of important organs.[1]

Sir Joseph Fayrer says that an attack beginning with fever may end with cholera, or *vice versa*. This is not surprising, for there is no reason for supposing that a person suffering from malarial fever should be exempt from cholera any more than from typhoid fever or from yellow fever. Nor, on the other hand, is it remarkable that one convalescent from cholera should be seized with intermittent or remittent fever in a malarious region. Dr. Sullivan insists that between "pernicious choleraic fever and Asiatic cholera it is almost impossible to diagnose." The same is true as regards Asiatic cholera and cholera nostras, and we suspect that "pernicious choleraic fever" is often nothing more nor less than the latter disease occurring in a malarial subject. It is only in India, where both cholera and malarial fevers are endemic, that the suspicion has arisen that these diseases are due to the same toxic agent.

An early diagnosis between algid pernicious fever and cholera—epidemic or sporadic—will depend upon the malarial history of the individual and the bilious vomiting, if vomiting occurs, in the one case, and upon the characteristic discharges and cramps in the other. The remittent character of the fever and tendency of the algid phenomena to return will serve to establish the diagnosis later.

Prognosis.—The mortality from pernicious remittent fever is largely influenced by the treatment, but under the most skilful treatment a fatal termination is not an infrequent result. Maillot, who prescribed quinine freely and fearlessly, but who had not the advantage of the hypodermic method of administering it, says: "The prognosis in pernicious fever is always very grave. The principal varieties—the delirious, the comatose, the algid—give nearly the same mortality." The mortality from the different forms as they occurred at Bona (in Algeria), which in Maillot's time was an intensely malarious locality, but has since been to a considerable extent reclaimed, was as follows:

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[1] Morehead, op. cit., p. 65.

> Ninety-nine cases of the remittent and pseudo-continued type furnished nineteen deaths—one in five, nearly; thirty-eight of these were of the comatose form and gave six deaths—one in six, nearly; twenty-six were of the delirious form and gave four deaths—one in six, nearly; thirty-five were of the algid form and gave nine deaths—one in four.[1]

Dr. Charles Parry, referring to "congestive fever" as it occurred forty years ago in Central Indiana, says:

> Without treatment, or with the usual treatment of bilious fever, which is little better than none in this disease, probably three-fourths of the cases terminate fatally. But with a special treatment not more than one in eight.[2]

Colin says that the mortality as given by various authors varies from fifty per cent. to one in five, which was about the proportion of deaths which occurred in his own practice in Rome—six deaths in twenty-seven cases. According to this author, the mortality is greater in the algid form and its varieties—cardialgic, syncopal, diaphoretic—than in the comatose;[3] the former occurring mostly in cachectic individuals who have suffered repeated attacks of intermittent, and the latter in newly arrived sthenic cases. Dr. Parry says that the plethoric, young, and robust are most apt to die. This was no doubt due to the fact that they are most subject to comatose attacks, and furnished a large proportion of the cases which came under his observation, for the algid form of the disease must have been extremely rare as far north as Central Indiana, even at the early day at which Dr. Parry wrote, when the virgin soil was being brought under cultivation.

The comatose form of pernicious fever occurs most frequently during the hottest season of the year, and the algid form in the autumn. According to Jacquot—and Colin agrees with this author—pernicious attacks occurring later than the month of October, either in Italy or in Algeria, are extremely rare and extremely fatal. Out of 886 cases of "pernicious fever" treated by Bailly in the civil hospital of San Spirito, Rome, 341 terminated fatally—about two in five. These figures, however, relating as they do to hospital cases, show a mortality far beyond that which should occur under proper treatment, for many cases are brought to a hospital in a hopeless condition. Colin says that when the pernicious attack was developed before the patient was brought to the hospital in his charge—in Rome—a fatal termination was the rule, and that three-fourths of the patients died. But when the pernicious symptoms appeared in cases already in the hospital, prompt treatment reduced the mortality to one in six. The comatose cases are especially fatal when neglected, and yet this form yields most promptly and easily to proper treatment.

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[1] Quoted from Bartlett, op. cit., p. 370.

[2] Am. J. M. Sc., July, 1843.

[3] Maillot also has verified the inferior gravity of the comatose variety (fourteen deaths in seventy-seven) and the deliriant (fourteen in sixty-one) as compared with the algid, in which the mortality was twelve in forty-eight. In Senegal the gravest form of pernicious fever was the algid, in which the mortality was as high as six out of seven cases (Archives de Méd., Feb., 1867, quoted from Colin, foot-note on p. 331).

The prognosis is extremely grave in those cases in which a similar attack has occurred but a short time before. Mayer says that second attacks are likely to occur within eight or ten days after the first, and that in his experience most of the fatal cases occurred in individuals attacked by pernicious fever a second or third time. Colin remarks that those who have once suffered a pernicious attack are extremely subject to subsequent attacks if not removed from malarial influences. At Civita Vecchia, in 1866, this author saw an officer attacked three times in succession with the comatose variety of pernicious fever at intervals of fifteen or twenty days, and he was with difficulty rescued from death.

Colin recognizes a choleraic variety of pernicious fever, which according to his experience is the least fatal of all the forms, no death having occurred in five cases coming under his personal observation. We venture to suggest the possibility that these were in truth cases of cholera nostras occurring in malarial subjects. As a result of his personal observations this author has constructed the following scale of gravity: "Commencing with the most benign, I would classify them in the following order: choleraic, icteric,[1] comatose, deliriant, cardialgic, algid, syncopal."

MORBID ANATOMY.—Pernicious *remittent* fever presents no special anatomical lesions differing from those already described in our article upon pernicious intermittent, and the reader is referred to this and to the post-mortem notes accompanying the appended cases for an account of the morbid anatomy.

CLINICAL HISTORY.—The pernicious forms of remittent fever correspond with those described in the article on pernicious intermittent fever, and there is little to add to the account there given, as the clinical features to which the term pernicious is applied are of the same nature whether the pyrexia have an intermittent or a remittent character.

The *comatose* form of the disease is that which is most frequently encountered in the United States, where it is very commonly known under the name of "congestive fever." This is also the most common form in malarial regions in other parts of the world, except perhaps in certain parts of India—banks of the Ganges—and in Cochin China, where the algid and choleraic forms are said to be more frequent (Colin). It seems probable, however, that this alleged exception to the general rule is, in truth, due to the prevalence of choleraic diseases in these regions. When an attack of "congestive fever" is immediately due to insolation, excessive fatigue, or alcoholism, acting in conjunction with malaria, coma may be suddenly developed without any premonitory symptoms—"apoplectic form." Fayrer gives the following as an example of the sudden development of malarial coma in a considerable number of individuals undergoing the same exposure:

> The severe action of malaria was observed by Mr. Eccles on the march of some troops from Larissa to Niccalla for two days and two nights, over a plain hemmed in by mountains, with two rivers running throught it, nearly dry in summer, overflowing in spring and winter, with rich marsh in the centre, and tributary streams. The men drank at muddy pools. On only the first night were they exposed to the dews, yet before their destination was reached three men had pernicious remittent; and on reaching Niccalla fifty men went into hospital with malarial poisoning, coming on so suddenly

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[1] This form, which corresponds with the *fièrre bilieuse melanurique* of other authors, does not properly come under the heading "pernicious remittent fever," according to the definition given in the present volume.

> that Mr. Eccles thought that they were cases of insolation. Six of them died in the first exacerbation. These he treated as for sunstroke. These cases occurred during the night and day after reaching Niccalla. The symptoms were: countenance livid; headache with vertigo in some, while others were comatose; great heat and dryness of skin; temperature 102° to 106°; full, hard pulse, sometimes rising to 120; dry and cracked tongue; vomiting; dyspnœa and tumultuous action of heart frequent. The fatal cases sank very rapidly in stupor, and two had convulsions. Noticing in one a slight remission Mr. Eccles gave twenty grains of quinine, and he found this most effectual. All the other cases were unsatisfactory.[1]

These sudden seizures are doubtless often due to the paralyzing action of the causes mentioned, quite independently of the immediate co operation of malaria, in individuals whose nervous centres are pigmented and enfeebled from previous malarial attacks. In this case it may be a question whether our diagnosis should be insolation, alcoholism, or malarial coma.

But pernicious symptoms of the same kind—cerebral congestion, delirium, and coma—due to the paralyzing influence of the malarial poison alone, may also occur during the course of a remittent fever. In this case the symptoms are developed during the height of the febrile exacerbation; algid phenomena, on the other hand, occur at the outset of an attack, during the cold stage or during a remission.

Cases of "congestive fever" are commonly preceded by the usual premonitory symptoms—lassitude, pain in head and loins, loss of appetite, irregular pulse, chilly sensations, etc.—followed by a brief cold stage, which is succeeded by intense febrile reaction, attended with cephalalgia, flushed face, injected conjunctivæ, hurried respiration, bilious vomiting, etc. The severity of the attack is shown by the excessive pyretic action—temperature often above 106°—and sometimes by delirium or coma occurring during the first exacerbation. Usually, however, one or more remissions occur before the pernicious character of the attack is manifested. At the moment when reaction is at its maximum the cephalalgia gives place to somnolence passing into stupor, the limbs become relaxed, sensibility is lost, respiration becomes labored and noisy, and the patient lies in an unconscious condition. According to Colin, sensation is rarely completely extinguished, and the patient may indicate by the expression of his face that he is conscious of pain, although it is difficult to arouse him sufficiently to obtain a response to a question. Sometimes there is simply dulness of intellect and a disposition to sleep during one or more exacerbations, followed by complete coma in a subsequent one. In some instances coma is preceded by delirium of a violent nature, and these cases have received a special designation—"*fièvre pernicieuse délirante*" (Colin); but as in fatal cases presenting this symptom the delirium passes into coma, it seems quite unnecessary to describe this as a special form of pernicious fever. When the patient, after being somnolent or delirious, passes into a condition of complete coma, his condition is one of extreme peril, and unless rescued by prompt treatment the case is very likely to terminate fatally. A more moderate degree of cerebral congestion, giving rise only to dulness of intellect or to partial coma, may disappear during the remission, and the inexperienced physician might imagine that his patient was out of danger. But unless the patient is in the meantime brought fully under the influence of quinine, pernicious symptoms of a more decided and commonly fatal character are almost sure to reappear during the next febrile exacerbation. Occasionally coma is preceded by convulsive seizures of a tetanic nature. This is a comparatively rare occurrence, but is recognized by some authors as a distinct clinical variety of pernicious fever—*fièvre pernicieuse convulsive* (Colin).

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[1] Fayrer: op. cit., p. 116.

> Dr. Boling, of Montgomery, Ala., has noticed cases of remittent fever in which the morbid innervation took the character of tetanic spasms. After a few febrile exacerbations, the approach of the paroxysm was marked by the occurrence of spasmodic phenomena exactly resembling those of an attack of tetanus, which afterward continued, increasing and diminishing in general with the exacerbations and remissions of the fever until the close. In some instances there was complete stupor or coma throughout the remainder of the disease; in others, only during the paroxysms, and in most some degree of intelligence remained. In no case did the disease extend beyond the fifth day after the supervention of spasm; and usually if not arrested it ended fatally at an earlier period. The result was generally unfavorable.[1]

Dr. Sullivan, whose observations were made in Havana, gives the following account of "comatose pernicious fever."

> The cold stage is absent but the hot stage is soon developed, and unlike the skin in febris algida, *it is bathed in a hot perspiration*—a frank intermittent is seldom observed. The fit may last from four or five hours to as many days. The characteristic symptoms are: loss of motion, sensation, and intelligence, with impaired function of respiration and circulation. The patient answers peevishly or in monosyllables; the pupils are insensible to light; some low murmurs of complaint may often be heard, indicating severe headache. The frequent return of motion proves the intermittent character, when the symptoms generally improve; but in cases which end fatally we may observe muscular contractions, tonic and clonic, and death closes the scene *after one or two attacks of black vomit.*[2]

Fergusson also speaks of black vomit as a common occurrence in pernicious fever in the West Indies. He says that "it often happened to a well-seasoned soldier, mounting the night guard in perfect health, to be seized with furious delirium while standing sentry; and when carried back to his barracks on Monk's Hill, to expire in all the horrors of black vomit."[3]

Notwithstanding the extended experience and high character of these observers, we venture to doubt whether these were uncomplicated cases of pernicious *malarial* fever; for, so far as we are aware, black vomit does not occur in cases of "congestive fever" outside of the endemic range of yellow fever, except in regions subject to occasional invasion by this disease, and at the time of such epidemic invasion.

The *algid form* of pernicious fever occurs most frequently in the autumn, and the victims of chronic malarial poisoning are especially subject to attacks of this kind, which seem to be induced by the intense action of malaria, independently of any accessory cause, acting upon an enfeebled nervous system. Those previously exempt from malarial attacks may, however, be seized with algid pernicious fever after an exceptionally dangerous exposure, as, for example, in the deadly *Terai* of India.

The algid phenomena may appear at the outset of an attack or may occur in the course of a simple intermittent. The algid condition is commonly regarded as an exaggeration of the cold stage, but according to Maillot, it is during the stage of febrile reaction that the symptoms which characterize this condition are developed.

> Often they appear suddenly in the midst of a reaction which appeared to be open and frank. The pulse becomes slow, flags, and disappears; the extremities, the face,

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[1] Wood's Practice of Medicine, vol. i, p. 307.

[2] John Sullivan, M.D.: The Endemic Diseases of Tropical Climates, London, 1877, p. 62.

[3] Quoted from Chevers: On the Ordinary Diseases of India.

> and the trunk become successively and rapidly cold; the abdomen alone preserves a slight degree of warmth, the skin feels cold as marble; the tongue, whatever may have been its appearance at the commencement, becomes flat, white, moist, and cold; there is no thirst, and if the patient is induced to drink, the liquid is frequently returned by regurgitation; the lips are colorless, the breath cold, and the voice broken; the action of the heart is slow, feeble, and struggling, appreciable only by auscultation, the mind is unimpaired.[1]

Colin also says that the algid condition results from an excess of the febrile movement, instead of being an exaggeration and prolongation of the cold stage, as Trousseau, Piorry, and others have asserted. According to this author, the algid phenomena are largely due to paralysis of the muscular fibres of the heart, resulting from excessive pyrexia (op. cit., p. 250).

No doubt in a certain proportion of the cases collapse occurs during or at the termination of an intense febrile exacerbation, as described by the authors quoted; but the pernicious symptoms may also appear during the initiatory stage. In such cases, to use the language of Dr. Dickson:

> The system seems to sink at once prostrate before the invasion or exacerbation, which can scarcely be called febrile. Reaction, to use our technical phrase, does not take place, or very feebly, if at all. The skin is cold and covered with clammy sweat as in the collapse of cholera; the pulse is weak and fluttering, the stomach is very irritable, with frequent and painful but usually ineffectual efforts to vomit; the countenance is shrunken, pale, and livid; there is often low, muttering delirium, with shivering and fainting. In some cases no complaint is made, a lethargic insensibility seeming to oppress the patient; in others the most extreme anguish is endured by the miserable sufferer, who in his agony utters groans or loud cries. The vital powers are speedily and irrevocably exhausted by the recurrence of a few exacerbations, although the remissions in this class of cases are usually well defined and full of transient relief and hope The third, fourth, or fifth return of the train of symptoms delineated, for the most part, puts an end to the distressing scene.

This account, which we copy from Dr. Davidson's valuable article on "Pernicious Fever,"[2] is no doubt a true clinical picture of a considerable proportion of the cases which fall under the observation of physicians within the limits of the United States, but according to the French authors above quoted, the algid condition frequently persists for several days without any such periodic amelioration of the symptoms as is described by Dr. Dickson.

Colin, in remarking upon the case which we have transcribed to our pages (page 279), says:

> We see that in this case the algid condition lasted three days; like the pernicious phenomena previously described – coma, delirium—algidity, then, is not transitory; and in speaking of an algid attack we do not refer to morbid phenomena lasting a few hours, as in intermittent fever, but to a condition which may persist for several days without offering any indications of periodicity.

Maillot also gives evidence of the same kind. He says:

> I have never seen the symptoms which characterize algid fever assume a periodic character; scarcely have they at times presented appreciable remissions, and I have not been absolutely certain of this. They have seemed to me, when once established, to progress continuously toward death, unless controlled by treatment.[3]

TREATMENT.—The fatal tendency of the form of disease under consideration is indicated by the title—pernicious—which medical authors generally agree in giving it. Without treatment "congestive fever" is a frightfully fatal disease, and by spoliative treatment—bleeding and purging—the fatal tendency is increased rather than diminished.

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[1] Quoted from Bartlett, op. cit., p. 356.

[2] N. O. Med. & Surg. J., Feb., 1880.

[3] Op. cit., p. 35.

Fortunately the victims of these pernicious attacks may in many cases be rescued from the jaws of death by a prompt resort to the use of our sovereign remedy in malarial diseases, administered in efficient doses and by a method which ensures its absorption. The same treatment will be effectual in preventing the development of pernicious symptoms when we have any reason to anticipate their occurrence. In the present state of knowledge it may be pronounced criminal to delay administering quinine, with the idea that some other measures may take the place of this remedy, at least for the immediate relief of the threatening symptoms.

The life of the patient is in our hands, and we have the experience of the past to guide us. This demonstrates conclusively that bleeding, purging, and blistering are inadequate for the relief of malarial coma, and that stimulants internally and heat and rubefacients to the surface do not cure algid pernicious fever. No doubt there are cases in which a few leeches applied to the mastoid processes may have a beneficial effect, and when the bowels are confined it is always well to give a purgative enema in the comatose and delirious cases. Cold applications to the head, when indicated, and revulsion to the extremities by sinapisms, hot mustard foot-baths, or friction with stimulating liniments, are valuable resources. In the algid condition the external application of dry heat and friction may help to restore the circulation. But all of these measures are secondary, and, independently of the use of quinine, they are commonly futile, or at least give only temporary relief, to be followed by a recurrence of the pernicious symptoms during the next febrile exacerbation, unless in the meantime the patient has been brought fully under the influence of the specific remedy. It would be an unnecessary repetition to go more into detail with reference to the treatment of pernicious remittent fever. It does not differ from that recommended for the corresponding pernicious forms of intermittent fever. Several of the cases which we give below also give the details of treatment as carried out by some of the most experienced practitioners in our own and in other countries. These cases have been carefully selected, and we believe that they will be found not the least instructive portion of the present volume.

CASES.—The two following cases are reported by Dr. J. Forsyth Meigs in his valuable paper already referred to :[1]

Pernicious Fever—Hypodermic Use of Quinia—Recovery Rapid.—Noah D——, aged twenty years, sailor. Admitted September 12, 1865. He left Philadelphia August 1, 1865, and went to Savannah; left that city September 3d; reached Philadelphia again September 11th. Was taken ill on the way up, September 5th; had one chill; afterward continued fever with remissions. Bowels loose; frequent vomiting and anorexia; no epistaxis; skin very dusky. He asserts that it became so after an attack of yellow fever in Cuba three years ago. Has been confined to bed for three days, as he struggled to keep up for the first four. On admission his symptoms were hebetude and restlessness; tongue very dry; face congested; capillary circulation torpid; bowels freely opened, large thin stools; frequent vomiting, especially provoked by quinia; pulse 120, very small; surface hot, but with tendency to be cold and shrivelled on extremities; voice feeble; spleen enlarged; abdomen large and tender, especially over liver; conjunctivæ yellowish.

September 13th.—Frequent vomiting; tongue heavily coated; hebetude. Urine acid, sp. gr. 1023; chlorides very deficient; no albumen; reddish-yellow with heavy deposit.

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[1] Pennsylvania Hospital Reports, vol. i., 1868.

September 14th.—Expression better; surface still dark; tongue heavily coated, merely dryish; eyes cholæmic; skin sallow; pulse 92, more volume; bowels opened once, not very thin; vomiting rare; slept quite well; anorexia; great thirst; temperature in axilla (11 A.M.) 102°. Respiration somewhat sighing. Urine acid; chlorides deficient; no albumen; reddish-yellow.

September 16th.—Slept well; nausea, but no vomiting. Bowels quiet; tongue heavily furred. Pulse weak, 72 per minute. Considerable hebetude; skin inclining to be cold and clammy on arms and legs. Anorexia.

September 18th.—Has very rapidly convalesced, and leaves the hospital, but is not in fit condition to travel. Urine acid; no albumen; chlorides still very deficient; color yellow.

Treatment.—September 12, 1865, 6 P.M.: On admission, whiskey, ℥j., and, if possible, quiniæ sulph., gr. xl.

September 13th.—Quiniæ sulph., gr. xl., gr. xx. of which were given hypodermically; mustard to stomach; tr. opii., gtt. lx., per anum; pil hydrarg., gr. iij., liq. ferri peracetatis (Basham's mixture), fʒss., q. q. h. Quiniæ sulph., gr. xij. by mouth; gr. xviij. hypodermically.

September 15th.—Quiniæ sulph., gr. xxiv. by mouth; 16th, gr. xviij.; 17th, gr. xij.; 18th, gr. ix. No irritation was produced in this case by the hypodermic use of quinine in concentrated solution.

Pernicious Remittent Fever—History of Debauch—Collapse—Slow Reaction—Gradual Recovery—Hypodermic Use of Quinia.—Thomas W——, aged forty-four, native of England. Admitted to the Pennsylvania Hospital September 13, 1865. First enlisted in the army December 10, 1861, and served twenty months; always in good health. Re enlisted March 6, 1865, in Tenth Corps. Has been in North Carolina, at Raleigh and Halifax; last at Weldon, for two weeks. Left there August 26th; reached Camp Cadwalader, Philadelphia, September 2d. Drank very freely on the way to this city, and for two or three days after arriving. First felt sick September 5th. Has not had any regular chill, but great prostration, with irregular exacerbations and remissions; sweats once or twice; constant vomiting; considerable purging.

On admission surface was cold and clammy; skin on extremities shrivelled; tongue dryish, moderately coated; skin sallow; eyes icterode; belly tympanitic; no eruption; liver and spleen enlarged and tender; constant vomiting, provoked by anything swallowed. One liquid stool soon after admission. Considerable deafness; profound prostration; pupils small; vision dim; expression of eyes wild; wandering delirium.

September 14th.—Prostration profound; tongue dryish, coated; pulse 95, very small; pupils contracted; no actual delirium, but stupor; quite deaf; roused with difficulty; memory weak; constant vomiting of thin yellowish fluid; bowels quiet; urine retained.

September 15th.—A very slight reaction occurred last evening. This morning his skin is less cold and damp; pulse 100, still very weak; less vomiting; urine still retained, not albuminous, chlorides absent.

September 16th.—Decided reaction; skin warm and supple; vomiting somewhat checked, a little lime-water and milk being now retained; pulse 90, very weak; bowels opened freely.

September 17th.—Vomiting has ceased; tongue less dry; some appetite; pulse 85, stronger; hearing better, and sight less dim; bowels regular.

September 18th.—Stomach bears Liebig's soup, milk punch, and quinia without vomiting. He is still very weak and has a good appetite. Warmth of surface normal; tongue moist and cleaning; hearing and sight much better.

September 20th.—Rapidly improving; still pale and weak; marked redness at the seat of several hypodermic injections; urine acid, sp. gr. 1013; no albumen; chlorides slightly deficient; color reddish-yellow.

September 22d.—Tumefaction of glands in left groin; slight febrile disturbance.

September 26th.—Lanced small abscesses in right and left groin, over seat of injections; color improving; still very weak; urine acid. sp. gr. 1016.

October 9th.—A few days after last note the incision in his right groin was extended and the wounds are now doing well. Steadily improving in strength and appearance.

Treatment.—September 13th (day of admission), quinia being rejected both by stomach and rectum, gr. x. were given hypodermically at 4, 5, 6, and 7 P.M. [The solution was of strength of gr. xx. to fʒj. of water, with enough strong sulphuric acid (gtt. ij. ad. iij.) to dissolve it.] As much beef-tea and whiskey as the stomach would bear—scarcely any. Tr. opii, gtt. lxxv., per anum. Blister over stomach; dressed afterward with morph. acet., gr. ss.

September 14th.—Hypodermic injections of quiniæ sulph., gr. x., at ten, eleven, and twelve. External heat and frictions. Enemata of milk punch f ℥ iij. and yolk of one egg every second hour.

September 15th.—Hypodermic injections of quiniæ sulph., gr. x., at nine and ten. Epigastric blister, dressed with morph. acet., gr. ss. Nutritious enemata continued.

September 16th.—Hypodermic injection, gr. x., at 9 A.M. The same on the 17th.

September 18th.—Stomach bears quinia; grs. iij. were given at nine and ten. Nutritive enemata given only every four hours, since he is able to take a considerable amount of milk-punch and beef-tea by the mouth.

September 20th.—Emp. ammoniaci cum hydrarg. applied over seat of one of the hypodermic injections on right pectoral muscle. Lead-water and laudanum applied over groin, as the superficial lymphatics are considerably enlarged, especially on the left side, where extensive suppuration, with some sloughing, has taken place. The other points of irritation were trusted alone. ℞. Tr. ferri chloridi, gtt. xx., q. q. h This was well borne by the stomach. Spts. frumenti, f ℥ xij. per diem. Quiniæ sulph., gr. vj. per diem.

October 9th.—Continues to take iron. Stimulants have been steadily diminished, and he now does not take any. The points of suppuration are healing kindly as his nutrition improves. Only three of the injections have caused suppuration; considerable irritation followed all the others, with some little tumefaction, but gradually subsided. That in the left groin is the only one where the suppuration has been at all deep and extensive; it laid bare the inguinal lymphatics. He still takes quiniæ sulph., gr. vj., each day. Is sitting up, much improved in appearance and strength.

He soon afterward left the hospital, almost entirely recovered.

In contrast with this favorable result in two severe cases in which the administration of quinine in full doses and a general supporting regimen constituted the entire treatment, we call attention to the following cases reported by Morehead, in which bleeding and purging had a prominent place in the treatment. It must be understood that these cases, although reported by Dr. Morehead, were not treated by him, and that he has expressed, in the most emphatic terms, his disapproval of blood-letting, catharsis, and mercurial treatment in such cases.

Remittent Fever in a Man of Intemperate Habits—Fatal, with Convulsions, Coma, and Tumultuous Action of the Heart—Considerable Effusion of Serum in the Head—Streaked Redness and Softening of the Mucous Membrane of the Stomach—Deep Red Tint of the Endocardium and Muscular Tissue of the Heart.—James R——, aged twenty years, a boiler-maker of stout habit, and a few months resident in India, was admitted to the European general hospital on July 2, 1838, affected with mild febrile symptoms. He stated that for several days previously he had suffered from a sense of oppression of the chest which he had attributed to cold, but which did not prevent him from following his occupation of boiler-maker. It was subsequently ascertained that he was a man of intemperate habits, and that he had been drinking to excess before his present illness. On the morning of the 3d, after a restless night, the skin was warm and soft, pulse soft and of natural frequency, tongue slightly furred in streaks, thirst considerable, no uneasiness of the chest or fulness of the abdomen. About 6 P.M. there was tenderness of the epigastrium, pulse frequent, hard, and sharp, manner excited and skin hot. *He was bled but fainted after the loss of sixteen ounces of blood.* Ten grains of calomel with a quarter of a grain of tartar emetic and a similar quantity of opium were given. During the night the bowels were frequently moved, and the evacuations were green and watery. On the morning of the 4th the skin was warm and soft, pulse 80 and firm, tongue moist and little furred, no excitement of manner. Five grains of calomel and twelve grains of Dover's powder were given. At the evening visit he felt better, the bowels had been twice moved, and the evacuations were dark and bilious. He was ordered a warm bath and a powder of chalk and mercury with Dover's powder. The night was passed without sleep; skin cool. Cold affusion was used, and he took during the daytime two doses of antimonial mixture with one drachm of tincture of opium. Sleep did not result, and after the evening visit the cold affusion was again used, and a draught with one drachm and a half of tincture of opium was given. He slept for several hours, but on the morning of the 6th he continued nervous and agitated, and the action of the heart and of the carotids was strong. He was directed to be cupped on the cardiac region; but while the operation was being performed he was seized with convulsions and died comatose after about an hour.

Inspection Six Hours after Death.—Much of the external integuments was of a purple tint. *Head:* There was considerable effusion of serum at the base of the skull and between the membranes of the brain. *Chest:* There were old costal adhesions and considerable infiltration of the lungs. The lining membrane of the heart and also the muscular tissue were of a deep red tint. The valves were healthy. *Abdomen:* The substance of the liver was paler than natural and variegated here and there with large spots of dark red. The mucous coat of the stomach was streaked dark red and softened. The spleen was soft and large, and the kidneys were normal.

Remittent Fever in a Man of Intemperate Habits—Death by Coma—Increased Vascularity of the Membranes of the Brain and Considerable Effusion of Serum—Softening and Vascularity of the Mucous Coat of the Stomach and Large Intestine—Commencing Degeneration of the Kidneys.—The commander of a merchant brig, aged forty-seven years, of intemperate habits, was brought to the European general hospital on July 13, 1838. It was stated that he had been feverish for some days, and had been drinking to excess. On admission he labored under mental illusions, but when his attention was kept fixed on one subject he answered questions rationally regarding it. There was no tremor either of the hands or tongue. After cold affusion and a draught with a drachm of tincture of opium and a third of a grain of tartar emetic, he became composed but did not sleep. The tongue was clean and the pulse frequent toward night. The bowels were freely moved but the pulse became feeble. Stimulants were substituted for the antimonial, and after the second dose he slept several hours. On the morning of the 14th the hands and tongue were tremulous, skin natural, pulse 96, full and soft. Camphor mixture with diffusible stimulants was directed to be given every second hour. Toward noon the skin became hot, the pulse increased in frequency, the tongue became dryish and more tremulous, and the delirium and general tremors increased. Twenty-four leeches were applied to the temples, and at 8 P.M. a blister to the back of the neck, and a draught with two drachms of tincture of opium was given. An hour afterward he fell asleep. In the middle of the night the pulse became thready. He was roused with difficulty, then became completely comatose, and died at 10 A.M. on the 15th.

Inspection Five Hours after Death.—*Head:* There was much vascular congestion of the pia mater, with considerable effusion of serum between that membrane and the arachnoid, and also into the ventricles. *Chest:* The lungs did not collapse. The heart was flabby and filled with fluid blood. *Abdomen:* The liver was of dark gray color and softened. The mucous coat of the stomach and large intestines was vascular and softened. *The spleen was enlarged and reduced to a bloody pulp.* In both kidneys the distinction between the tubular and cortical substance was ill-defined.

Dr. Morehead remarks with reference to these cases that the influence of intemperate habits is apparent; that the remissions were well marked, but that no advantage was taken of them in the treatment—*i.e.*, quinine was not given—and that the opiate was injudiciously given. The following case is from the same source:

Remittent Fever Proving Fatal by Collapse and Coma at the Close of an Exacerbation—No Serous Effusion in the Head—Dotted Redness and Softening of the Mucous Membrane of the Stomach—Enlargement of the Mucous Follicles of the Colon and of Peyer's Glands.—George C——, aged twenty, a seaman of stout habit, was admitted into the European general hospital June 23, 1838. He stated that he had been ill with fever for five days, during which time there had been headache and occasional vomiting. On admission his manner was sluggish, skin hot, pulse 120, full but compressible, tongue furred and expanded. *Six dozen leeches* [1] were applied to the temples, and pills of extract of colocynth, calomel, and tartar emetic were given. On the 24th the head, though relieved, was still uneasy, the skin was cool and moist, pulse 120 and feeble, the abdomen was soft, and during the night there had been seven watery bilious evacuations. A *blister* was applied to the back of the neck, which rose well but caused strangury. At the evening visit there was less sluggishness, the skin was cool, pulse 120, soft, the bowels had been freely moved, and the tongue was cleaner. Draughts with nitrous ether were ordered, and pills of blue mass and ipecacuanha. The night was passed without sleep.

On the 25th questions were answered freely but giddiness was complained of. There was also uneasiness across the umbilicus, and there had been several ineffectual calls to stool; thirst moderate, tongue more furred and expanded. Compound powder of jalap was given with ether and camphor mixture. At the evening visit it was reported that he had slept, the skin was cool and moist, and no medicine was given. During the early part of the succeeding night he rested well, but toward morning there was a return of slight headache, increased by motion, with some intolerance of light and flushing of the face. The skin was cool but dry, pulse 100, soft and of good strength, bowels freely opened, the tongue less furred but somewhat florid at the edges. *Six dozen leeches* were applied to the temples, and a diaphoretic draught was given every three hours. At the evening visit the head was easier and the skin cool and moist. The succeeding night was passed without sleep, and at 3 P.M. of the 27th there was a febrile exacerbation followed by much *collapse* in the night-time. *He became comatose and died* at 7 A.M. of the 28th.

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[1] Italics by the present writer.

Inspection Five Hours after Death.—Head: There was no increased vascularity of the membranes or substance of the brain. There was about a drachm of serum in the left lateral ventricle, and about half an ounce at the base of the skull. *Chest:* With the exception of some old costal adhesions, the thoracic viscera were healthy. *Abdomen:* The liver was healthy and the gall-ducts free. The mucous lining of the cardiac end of the stomach for a space larger than the hand was of dark red color, dotted, marbled, and its texture softened; toward the pyloric end the color was natural, but the tissue was softened. The small intestines were filled with lumbrici. The aggregated glands of Peyer were enlarged. The mucous coat of the cæcum and colon was of a dark gray color, and studded throughout with dark points (enlarged follicles).

Dr. Morehead remarks with reference to this case that it is the only one of which he has notes in which head symptoms occurred during life without morbid appearances in the head after death. Of the treatment he says that it was defective in the neglect of quinine during the remissions and too much depletion in the exacerbations. "The appearance of the mucous lining of the large intestine indicated an undue use of irritants."

The following case is given by Dr. Chevers, and we introduce it here as an illustration of the paralyzing influence of the malarial poison and its malignant potency independently of any such accessory cause as alcohol:

Mr. Hare describes as the worst case he ever saw that of Assistant Surgeon W——, a strong, active man, and celebrated for the fatigue he could undergo in shooting. Dr. W. was delayed for one night in the Terai at the foot of the Nynee Tal Hills, and on his arrival at Simla had all the symptoms of delirium tremens, so much so that many thought, though he was a strict water-drinker, that he was suffering from intemperance. This strong, healthy young man, from a few hours' exposure, became blue and livid; he staggered when he attempted to stand, his hand and tongue were tremulous, his eye dull, and though he moved about he seemed unconscious of what he was doing, and he died after some days with coma.[1]

The following cases are reported by Colin (op. cit.):

Comatose Remittent Fever.—B——, private Nineteenth Infantry; in Italy two years; stationed in the quarter Saint-André della Valle; not previously admitted to hospital. Admitted to my wards in the Hospital Saint-André at the moment of my morning visit. The previous evening, his comrades say, he had violent pain in the head and loins, and vomiting, then went to bed and snored like a drunken man: passed urine in bed. This comatose condition, which still persists, has therefore lasted about twelve hours. The skin is hot, the face flushed, the conjunctivæ injected, pulse 120, respiration noisy; sensation very obtuse, but not completely abolished; frequent efforts to spit, alternating with grinding of the teeth and trismus. We were able, however, to provoke movements of deglutition, and caused him to swallow in our presence fifteen decigrammes of sulphate of quinine. Twenty leeches were applied to mastoid processes and sinapisms to the calves of the legs. At the time of our evening visit the fever and coma still persisted; vomiting reappeared at noon, about four hours after taking the sulphate of quinine; trismus more complete; absolute insensibility; respiration noisy, more frequent, but without tracheal râles. *Prescription:* Twelve leeches to mastoid processes; an opiate enema containing 2 grm. of sulphate of quinine (retained about half an hour).

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[1] Medical Times & Gaz., Ap. 14, 1883.

July 22d.—There is at present only somnolence and profound stupor; the patient, who does not believe himself in hospital, replies to questions slowly and in a surprised manner; the pulse is 100; the skin yet very hot; the pains in the head and loins are so severe that he cries out constantly; tongue coated, thirst intense. *Prescription:* A potion containg 2 grm. of ipecac. At our evening visit there was a notable amelioration; the skin was a little moist, pulse 84. *Prescription:* One gramme of sulphate of quinine and a potion containing ether.

Convalescence rapid without accident. Discharged August 14th.

Remarks.—In this case coma occurred on the second day of sickness, at the moment when the febrile movement was at its maximum, and it lasted nearly forty-eight hours. It disappeared suddenly with the fever, and convalescence pronounced itself as frankly as in the benign forms. We remark that in the treatment we resorted immediately to antiphlogistics and to the sulphate of quinine, the gravity of the case not permitting us to commence by evacuant medication.

In other cases coma manifests itself more promptly, suddenly even in the midst of exercise, of exaggerated fatigue, still more frequently under the influence of insolation. The following case is a remarkable example of this:

Comatose Remittent Fever, induced by Insolation.—W——, grenadier Nineteenth Infantry; in Italy two years; not previously sick; is stationed in one of the most notoriously insalubrious quarters of Rome, at the Convent of San Giovano Decollato. August 2, 1864, at three o'clock in the afternoon, he was sent with one of his comrades to the abattoir, situated at the other extremity of the city (near the gate del Popolo) to obtain the meat for distribution to his company. While on the way he complained of a violent headache and fell unconscious in the open street, and was transported to my wards in the military hospital of Saint-André (No. 47). The physician on duty at once applied twenty leeches to the mastoid processes and succeeded, notwithstanding a very decided trismus, in introducing into his mouth a solution of 15 degr. of sulphate of quinine, a part of which was swallowed and the remainder rejected by spitting.

August 3d.—At our morning visit we saw the patient for the first time; coma had then lasted for sixteen hours; respiration had been noisy during the entire night; the mouth was open, the tongue black and dry; the nostrils fuliginous; skin hot; pulse frequent, but compressible and irregular; urine passed involuntarily. *Prescription:* Twenty leeches; 15 degr. of sulphate of quinine. The same day at the evening visit the patient remained simply stupid; the pulse had fallen to 96 and was regular; thirst and headache intense. *Prescription:* One gramme of sulphate of quinine, a potion containing ether, sinapisms to the calves of the legs.

August 4th.—Has had a restless night, and it was necessary to tie him to the bed because of his constant attempts to get up and go to his quarters. Skin hot; pulse 100; violent cephalalgia, bilious vomiting; constipation since admission. *Prescription:* Two grammes of ipecac; purgative enema.

August 5th.—Notable diminution of the fever; subicteric tint of sclerotics and of the *alæ nasi.* Tongue very much coated, yellowish; great thirst; pain in the entire dorsal region. *Prescription:* Seidlitz water; thin bouillon. The following days icterus became a little more pronounced, but the general condition rapidly improved.

August 23d.—The patient received half-diet. At this date he was attacked with a perfectly well-marked quotidian intermittent fever, which yielded the fourth day to very moderate doses of sulphate of quinine. The patient was sent, convalescent, to France September 5th.

Coma in this case was determined by insolation; but, as we have previously remarked in cases of this kind, the patient, inhabiting an insalubrious quarter, had a predisposition to accidents of this kind. And notwithstanding the abruptness of the seizure, gastric phenomena were developed here as in the simple forms. The attacks of intermittent fever, occurring during convalescence, indicate very clearly the malarial nature of the affection.

In the following case a similar seizure resulted eventually in death from chronic meningitis. Colin suggests that this may have been due to the delay in resorting to antiphlogistic treatment. However this may be, the case serves to illustrate the fact that simple hyperæmia attended with coma may in these cases result in inflammation of a chronic nature.

Comatose Remittent Fever—Death.—K——, grenadier Fifty-ninth Regiment; in Italy two years. Attacked July 11, 1866, with violent pains in the head and loins and bilious vomiting. He received in quarters an emetic and a dose of sulphate of quinine. The following day, according to his comrades, he manifested some confusion of ideas, and when brought to the hospital, July 15th, had been completely unconscious since the previous evening. At the moment of our visit (fourth day of sickness) his skin was hot; pulse full and frequent; respiration noisy; limbs relaxed; insensibility absolute; stools involuntary. *Prescription:* Twenty leeches to mastoid processes; 15 degr. (about 23 gr.) of sulphate of quinine in solution. At the evening visit there was a slight diminution of the febrile movement; pulse slow, very full; sensibility slightly restored; when the patient is spoken to in a loud voice, a slight recognition is observed in his look, but he does not respond. (Enema containing 1 grm. of sulphate of quinine.)

July 16th.—Considerable agitation during the night; tongue dry, fissured; pulse 90; decubitus upon left side, body curved as by a tetanic contraction. *Prescription:* Twenty leeches, sinapisms, purgative enema. In the evening the muscles were again relaxed; the pulse had fallen to 60, still full but very compressible; skin inundated with perspiration, almost cold at the extremities; face discolored and expressing profound stupor. (Bouillon, and potion containing 10 grm. acetate of ammonia.)

From this time until the day of his death, which occurred September 27th—nearly two months later—the patient had no more fever but all the signs of a general affection of the nervous centres; alternate contraction and resolution of the limbs, frequent vomiting, difficult deglutition, involuntary stools; the only constant phenomenon was an absolute muteism. At the moment of death, which occurred by asphyxia, emaciation was extreme, and a large slough had formed over the sacrum.

Autopsy.—Head: Considerable serous effusion in the arachnoid cavity: thick fibrinous exudation along the sub-arachnoid vessels; adherence of the pia mater to the gray substance of the brain, which appeared bleeding and "*ulcérée*" when the membranes were removed. Ventricles empty. *Chest:* Frothy mucus in bronchi; hypostatic congestion at the base of both lungs. *Abdomen:* Intestine extremely pale. Liver pale, "*comme lavé*," without alteration of the hepatic cells. Spleen weighs 200 grm., completely softened; does not offer any noticeable pigmentation.

Malarial Cachexia—Pernicious Symptoms—Delirium, then Coma.—G——, private Eighty-fifth Infantry. Admitted to military hospital Saint-André, July 21, 1865, from civil hospital d'Orte. This man presented the appearance of a person with advanced malarial intoxication; complexion straw-yellow; considerable enlargement of liver and of spleen; anæmic murmur, etc. Has been in Italy three years, and was admitted to the civil hospital d'Orte because of an attack of tertian intermittent fever, of which the paroxysms have been arrested for six days. A supporting regimen was prescribed, and, as a prophylactic, two doses of sulphate of quinine (eight decigrammes) each week.

August 20th.—At the moment of our visit the patient got out of bed and came to join the persons who accompanied us, desiring, he said, to return to France with us (he had been proposed for a convalescent leave). He allowed himself without difficulty to be returned to bed, and when we asked an explanation, replied only by a burst of laughter. No change was made in his regimen, but we administered to him at once eight decigrammes of quinine.

August 21st.—At our morning visit this patient was found in a comatose condition, but without fever (apoplectic form), and without having been agitated during the night. *Prescription:* One gramme of sulphate of quinine and twenty leeches to mastoid processes. The same day at three o'clock coma still persisted; skin slightly moist, without heat; pulse 76; trismus had disappeared; sensibility had partly returned. *Prescription:* Potion containing 15 grm. of acetate of ammonia, frictions with vinegar, sinapisms, and purgative enema.

August 22d.—The patient has been conscious since last night; he is very feeble. No further accident occurred, and he was sent to France September 10th.

Remarks.—I attribute, in this case, the greatest importance to the preventive dose of quinine given August 20th, at the moment of my visit, in consequence of the delirious conceptions manifested by the patient. Without this precaution the comatose seizure of the following night might have been, without doubt, much more grave, and perhaps fatal.

Comatose and Convulsive Remittent Fever—Recovery.—T——, private Fourth Regiment of Hussars. In Rome one year. Admitted to the military hospital Saint-André, September 5th, at 8 A.M. This man was in apparent good health last evening; was suddenly attacked with intense fever and almost absolute loss of consciousness; there is violent contraction of the muscles of the jaw and of those of the legs, which are drawn up against the buttock and cannot be extended; from time to time there are clonic convulsions of the muscles of the right side of the trunk, causing sudden curvature of the body and necessitating the presence of an attendant to prevent the patient from falling out of bed. Respiration noisy, stertorous; face purple; dribbling of bloody saliva: stools involuntary. *Prescription:* Two grammes of sulphate of quinine by enema; twenty leeches behind the ears; sinapisms to the lower extremities.

The same day at three o'clock apyrexia was almost complete; the respiration was profound but calm; somnolence, but the patient responds easily to questions; no more convulsions.

September 6th.—The same satisfactory condition at the time of our arrival, but during our visit to the hospital the patient was again seized with convulsions and loss of consciousness without notable acceleration of the pulse or respiration. *Prescription:* Two grammes of sulphate of quinine by enema, and a potion containing 20 grm. of acetate of ammonia. The attack terminated at eleven o'clock, leaving the patient, as the day before, in a condition of profound stupor.

September 7th, at noon.—Return of convulsions with loss of consciousness; we prescribed at our evening visit 1 grm. of sulphate of quinine by the mouth, and an opiate enema containing 15 dcgr. of the same salt.

Somnolence continued for some days, augmented in appearance by the deafness due to the administration of the quinine. The patient was able to leave his bed September 11th, and recovered without any relapse. This case is remarkable by the frightful rapidity of the invasion, and, notwithstanding the tendency to relapse, by the prompt convalescence.

The following interesting case of algid pernicious fever is also reported by Colin:

Algid Remittent Fever—Death.—M——, private Fifty-ninth Infantry; in Italy four years; in hospital three times with intermittent fever. Admitted to the military hospital at Civita Vecchia, July 17, 1866. Has had an intense fever for two days, continued, without chills, attended with vomiting and intense cephalalgia, which causes him to cry out with pain. Skin hot; pulse 110; face turgescent; tongue coated and yellowish. *Prescription:* Two grammes of powdered ipecac; 15 dcgr. of sulphate of quinine to be taken at 3 P.M., in a potion containing ether.

July 18th.—The patient feels very well; the face is pale, and has taken a subicteric tint; but the most striking phenomenon is the coldness and cyanotic hue of the extremities, which are covered with a clammy and icy sweat. *Prescription:* Opiate enema containing 2 grm. of sulphate of quinine; potion containing 15 grm. of acetate of ammonia; vapor bath.

July 19th.—The algidity persists, but the patient has no sensation of cold; voice extinct; urine suppressed; intelligence perfectly normal. *Prescription:* Potion with camphor and opium, and 15 grm. of acetate of ammonia, sinapisms.

July 20th.—Tranquil delirium; face smiling; pulse almost imperceptible. Notwithstanding the renewed application of stimulants and of revulsives, the algidity augmented more and more, and the patient expired July 21st, at 6 P.M.

Autopsy.—Head: The meshes of the pia mater are distended with a transparent liquid, apparently gelatinous, which escapes with difficulty upon pressure. The substance of the brain is abnormally firm. *Abdomen:* Uniform congestion of the entire intestinal canal; stomach very red, especially along the greater curvature. Liver normal. Spleen double the normal volume (weighs 280 grm.); the capsule is thickened but the interior is very soft; in the interior of the parenchyma are two masses, the size of a pigeon's egg, which are entirely diffluent, and of which the dark color, due to accumulation of pigment, contrasts strongly with the rest of the parenchyma. Kidneys purple, enclosing in their pelves a yellowish liquid containing small granules of uric acid. The heart is yellowish and distended by an enormous quantity of soft and diffluent clots; hepatization of the inferior lobes of the lungs.

This case shows the futility of trusting to revulsion or to a moderate dose of quinine when a patient is in such imminent danger as was this soldier on the morning of July 18th. The prescription of 2 grm. (30 gr.)

of sulphate of quinine by enema proved entirely inadequate to relieve the vaso-motor paralysis, and the algid condition continued for more than three days without any further attempt to bring the patient under the influence of the specific remedy. In contrast with this sparing use of quinine we may call attention to the case reported by Dr. J. Forsyth Meigs (page 273), in which it was administered in doses of ten grains by the hypodermic method, at four, five, six, and seven o'clock on the day of admission to hospital; at ten, eleven, and twelve o'clock the following day; and at nine and ten o'clock on the next day. In all, 90 gr. in three days by hypodermic injection. Result, recovery.

COMPLICATED REMITTENT FEVER.

Under this heading we shall refer briefly to certain complications which are liable to occur in the course of a remittent fever, and which, whether due to an independent cause or resulting from the action of malaria, give rise to special clinical phenomena, and modify the treatment or the prognosis.

Pre-existing complications, such as tuberculosis, chronic Bright's disease, etc., cannot receive attention in the present volume. Nor can we consider those cases in which a fever of a remittent character is due to the combined action of malaria and other specific disease-poisons—*e. g.*, that of typhoid fever, yellow fever, etc.

Many of the cases included under the headings adynamic remittent fever and pernicious remittent fever doubtless owe their special characters to complications, and might with equal propriety have been described under the present heading. Thus scorbutis is a complication which gives an adynamic tendency, and chronic alcoholism a complication which gives a tendency to cerebral congestion and coma. The distinction between a case with cerebral complication and a pernicious comatose attack should properly be made to depend upon the presence or absence of inflammatory changes in the brain or its membranes. When such changes have occurred we have a case with cerebral complication; otherwise coma is simply a pernicious symptom depending upon vaso-motor paralysis and hyperæmia. But this distinction is much easier to make upon paper than at the bed-side, or even at the post-mortem table. We may assume, however, when the patient promptly recovers from the comatose condition, that it was due to hyperæmia alone; and when it persists for a day or more, and is recovered from very gradually, that more or less effusion has taken place. In fatal comatose cases some evidence of inflammation of the brain or of its meninges is usually found. So also with reference to gastro-enteric complications: the dividing line between simple hyperæmia of the gastro-intestinal mucous membrane—which is a common and perhaps constant accompaniment of simple remittent fever, and especially of "ardent fever"—and inflammation of the same membrane—which would constitute a gastric, or enteric, or gastro-enteric complication—is not always easy to make; for the dividing line is not sharply drawn. But on one hand we have cases of simple remittent fever attended with uncontrollable vomiting at the outset of the attack, in which this symptom is completely relieved during the remission, at which time the patient may be able to take food without distress, if without relish. Evidently the symptoms in this case are due to functional derangement of the stomach. When, however, we have persistent pain on pressure over the epigastrium, and persistent nausea and vomiting during the remission, with inability to retain the simplest liquid food or even cold water, we may be pretty sure that a gastric complication has been developed. In like manner tenderness over the bowels and discharges indicating an intestinal catarrh would establish the diagnosis of an enteric complication. A dysenteric complication, also, is made apparent by the character of the discharges; and a hepatic complication by tenderness on pressure over the region of the liver, etc.

It must be remembered that gastro-enteritis, dysentery, hepatitis, and other local inflammations may arise from causes independent of malaria, and are often attended with fever of a remittent type when they occur in malarial subjects. In this case we are not dealing with a remittent fever complicated with visceral inflammation of one kind or another, but with gastro-enteritis, dysentery, etc. This distinction is an important one, for in either case it is the primary disease which requires especial attention.

CEREBRAL COMPLICATION.—No doubt the cerebral symptoms in many cases of "congestive fever" depend upon other causes than the direct paralyzing influence of the malarial poison, and would properly come under the heading cerebral complication. This is especially true in those cases in which the seizure may be directly traced to insolation or to a debauch. But most authors include these cases under the heading congestive or pernicious fever when malaria is recognized as the remote cause of the attack, and we have followed their example. Morehead, however, considers delirium and coma occurring in the course of a remittent fever as a cerebral complication. He states that fully one-third of the fatal cases among European officers in the Bombay Presidency, India, were attended with such complication, and that the proportion was still larger among sthenic European soldiers.

According to this author, headache, delirium, and a flushed face occurring early in an attack are usually due to the direct influence of the exciting cause, and indicate an "active determination of blood to the brain and its membranes." The cases on page 275, which we have placed under the heading pernicious remittent fever, are given as examples of such active determination of blood to the brain in intemperate individuals. We hesitate to differ with so high an authority, but in our view the hyperæmia in these cases is due to the paralyzing influence of insolation or of alcohol, or of one or both of these causes combined with malarial poison, and the treatment is the same as in those cases in which coma is developed later from exhaustion of nervous energy; and in which, according to Dr. Morehead, "head symptoms very similar sometimes occur, after the fifth or sixth day, in cases in which the treatment of the remissions has been neglected and that of the exacerbations has been injudiciously depressant." Dr. Morehead thinks that it is a serious error to treat head symptoms thus arising in the same manner as those caused by "cerebral determination." This is no doubt true if depletion is the remedy for this condition. But is it not also a serious error to treat these head symptoms when they occur at the outset of an attack, as a result of the causes mentioned, upon the theory that they arise from "active determination of blood to the head?" Such a theory is likely to lead to a reliance upon depletion rather than to the administration of large doses of quinine, which experience proves is a far more successful mode of treatment. If in addition to this it is thought necessary to apply twenty leeches to the mastoid processes, as M. Colin is in the habit of doing, there is excellent authority for the practice, and we may be mistaken in thinking that this is rather a concession to the theories and therapeutics of the past than an essential part of the treatment of these cases.

The following case illustrates the danger of allowing a remittent fever to run on unchecked and the failure of leeching to prevent the development of coma:

Remittent Fever—Coma from Exhaustion.—A gentleman in the public service became affected with febrile symptoms at Tanna on September 4th. No treatment was adopted. He went to Bombay and remained there also without treatment, experiencing febrile accessions till the 8th, when he returned to Tanna. He had rigors on the boat two hours before landing. On the morning of the 9th there was remission, and toward evening an exacerbation, for which an emetic and a purgative of calomel were given. On the 10th at 4 P.M. there was again an exacerbation, with sense of swimming in the head. *Eight dozen leeches* were applied to the temples. There were rigors at midnight, followed by coma and death at 8 A.M. of the 11th.[1]

Cerebral symptoms resulting from inflammation of the membranes or of the substance of the brain are said by Morehead to be rare compared with those from simple "determination of blood"—hyperæmia. He reports, however, three fatal cases which came under his own observation. We select the following as the most instructive:

Remittent Fever Admitted after a Week's Illness—Head Symptoms Chiefly Marked by Unsteadiness of Manner, and latterly Drowsiness—Arachnoid Membrane Opaque and Thickened—Increased Serous Effusion.—William S——, aged sixteen years, after having been ill for a week with headache and fever, was admitted into the general hospital on May 9, 1842. There was heat of skin, flushed countenance, undecided manner. The tongue was yellow at the centre and florid at the tip, and the epigastrium was tender. Twenty-four leeches were applied to the temples and thirty-six to the epigastrium, the head was shaved, cold applications were used, sponging of the general surface had recourse to, effervescing draughts were exhibited from time to time, and some blue pill and ipecacuanha given at bed-time. On the morning of the 10th there was still heat and dryness of skin, but in other respects the symptoms were improved. In the evening there was a distinct febrile exacerbation. Sponging, cold applications, and effervescing draughts were continued, and the blue pill and ipecacuanha were repeated. On the morning of the 11th, still pyrexia, pulse 92, tongue slimy and tremulous, bowels rather relaxed, and manner unsteady. The remedies were continued, with addition of spirit. æther. nit. to the effervescing draughts and the application of a blister to the nucha. On the 12th febrile heat and other symptoms continued, accompanied with slight subsultus. Camphor mixt. c. spirit. æther. nit. was given every third hour, also chicken soup. On the 13th, pulse 104; four feculent dejections. In other respects as on the 12th. Sago and milk morning and evening, chicken soup for dinner, and the camphor mixture continued. On the morning of the 14th there was a distinct remission, and quinine and blue pill were ordered every second hour, with effervescing draughts. The evening accession was milder. On the 15th and 16th the febrile exacerbation seemed to be somewhat checked under the use of quinine; but on the 17th the symptoms were all again aggravated. On the 18th he vomited several times, and passed three copious watery evacuations, followed by sunken features, feeble pulse, and dampskin. These symptoms continued, with the addition of drowsiness, on the 21st, and death took place on the morning of the 24th.

Inspection Eight Hours after Death.—*Head:* The arachnoid membrane over the convex surface of the brain was opaque and thickened, with here and there small round granules of lymph the size of a pin's head. There was about an ounce of serum in the lateral ventricles, and about an ounce and a half at the base of the skull. The substance of the brain was firm. *Chest:* Old adhesions connected the right lung to the pleura; but the substance of the lungs was crepitating. Heart healthy. The colon distended, but its mucous coat healthy. The mucous coat of the stomach was of dark gray tint with dark red streaks, but was sound in texture.

We cannot question the diagnosis in this case, which came under Dr. Morehead's personal observation, but the clinical history and post-mortem notes might otherwise have justified a suspicion that it was one of tubercular meningitis, in which disease the pyrexia often has a remittent character. The disastrous result of waiting for a remission before administering quinine to cure the fever is well illustrated in this case.

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[1] Reported by Morehead, op. cit., p. 86.

Other examples of cerebral complication in which effusion of serum into the ventricles, increased vascularity, and sub-arachnoid exudation of lymph was observed at the post-mortem examination are given on page 275.

Dr. Morehead points out the fact that serous effusion is often found upon post-mortem examination in cases which presented no marked cerebral symptoms during life, and that, consequently, the inference that in other cases in which head symptoms were present, these were due to serous effusion—observed at the post-mortem examination—may not be well founded.

GASTRIC COMPLICATION.—Irritability of the stomach is one of the most constant symptoms of the invasion of simple remittent fever, and is commonly evidence only of functional derangement, of the presence of acrid secretions, or of hyperæmia of the mucous membrane. But when this gastric irritability persists, and is associated with tenderness on pressure over the epigastrium, and a tongue more or less florid at the tip and edges, there will be reason to suspect that gastritis has been developed, and this may properly be considered a complication. This complication is especially common in persons of intemperate habits; and, according to Dr. Morehead, frequently results from "the unnecessary use of calomel and purgatives in the hot stage."

When this complication exists it will be necessary to administer quinine for the cure of the fever by enema, or by hypodermic injection, and to give the inflamed organ absolute rest. Nothing should be taken into the stomach except bits of ice or small quantities of ice-cold water, and nutriment should be administered per anum. When it is thought that the stomach is able to resume its functions it should be carefully tested with small quantities of lime-water and milk, or chicken broth, and gradually with more substantial food. Much relief will often be given in these cases by the application of sinapisms to the epigastrium.

We prefer a simple rubefacient such as mustard or chloroform, which can be frequently renewed, to the application of a blister, which is itself a cause of fever and distress.

ENTERIC COMPLICATION.—The causes which produce acute or chronic diarrhœa are especially active in southern latitudes, and during the summer and autumn months, when remittent fever is most prevalent. It is, therefore, not surprising that these diseases are often associated. Moreover, the debility resulting from an intestinal flux increases the susceptibility of an individual to the action of malaria; and, on the other hand, the hyperæmia of the intestinal mucous membrane, which exists especially during the cold stage of a remittent fever, reduces the resisting power of this membrane to local causes of irritation, and increases its susceptibility to be injuriously affected by general causes, such as exposure to cold, etc. During the late war "it was exceedingly common for intermittent or remittent fever to coexist with diarrhœa in the same individual, the fever sometimes preceding and sometimes following the initiation of the bowel affection" (Woodward[1]).

Morehead says that, in his experience, diarrhœa has been a somewhat more frequent complication than dysentery, but that it cannot be said to be a common one, "for it was only present in 6 out of 114 clinical cases in natives" in India. In fatal cases in which increased alvine discharges have been present during life, evidence of enteritis will commonly be found at the autopsy.

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[1] Med. & Surg. Hist. of the War. Second Medical Volume, p. 287.

The treatment of this complication will not differ from that proper to the intestinal affection when it occurs independently—rest, liquid diet, sinapisms, and hot fomentations applied to the abdomen, opiates, and astringents (?). These remedies will, however, commonly prove inefficient so long as the primary disease is not controlled by specific medication; for the enteric complication, although not directly due to malaria, is aggravated by the daily febrile exacerbation and its attendant phenomena, and especially by the congestion of the abdominal viscera which results from the paralyzing action of the malarial poison.

DYSENTERY is an occasional complication of remittent fever; and the victims of chronic malarial poisoning are especially subject to this disease. As in other febrile diseases in malarial subjects, the pyrexia in acute dysentery is likely to have a remittent character, and the dysenteric symptoms in this case are subject to periodic fluctuation. Dr. Woodward says:

> The malarial influence appears to favor the development of simple inflammatory or catarrhal affections of the intestinal mucous membrane. I do not think that Virchow exaggerates very much when he affirms that almost all the febrile conditions which occur in swampy regions during the warm months, or during the prevalence of intermittents, are accompanied by such intestinal disorders, and that these are only too readily aggravated into dysentery. But undoubtedly, also, intestinal catarrhs which may or may not pass into dysentery are very readily provoked under the same circumstances in individuals in whom no febrile condition has been developed prior to their occurrence. If periodic fevers should subsequently set in, the flux not unfrequently also manifests a periodic type; but even when uncomplicated by the fevers, the fluxes of malarial regions sometimes exhibit more or less distinct periodicity. . . . During the war this complication was even more frequently observed than previously, because the great armies, moved suddenly from the Northern States into the malarial regions of the South, were exposed simultaneously to malarial influences and to the causes of dysentery. In the resulting compound, or hybrid forms of disease, the symptoms resulting from each cause often appeared together in the same individual from the beginning of the case to its end. Sometimes, however, dysentery, either of itself or as a sequel of diarrhœa, appeared as the primary disorder, assuming subsequently a periodic form, either as to the flux itself or as to the accompanying fever, or ague or remittent fever made its appearance during convalescence from dysentery, or after it had become chronic. In other cases the periodic fevers were the primary morbid condition, and dysentery alone, or preceded by diarrhœa, set in only after the health had been broken down by long-continued ague, or after remittent fever had first been developed.[1]

Dr. Morehead says that the occurrence of dysentery in the early or advanced stages of remittent fever in sthenic or asthenic constitutions has been a rare event in his experience. That dysentery when associated with remittent fever is a complication, and not one of the results of malarial poisoning, is very clearly shown by the observations of Colin. This author, while admitting that the two diseases are often associated where the causes of both are present, as in Algeria and in other tropical regions, points to the fact that at Rome, "where malaria reigns to such an extent as to absorb all other affections, dysentery is extremely rare."

The remarks made with reference to the treatment of intestinal catarrh also apply to this complication. The primary disease is to be arrested as promptly as possible by the use of quinine; and for the control of the dysentery we must rely mainly upon rest, opiate and emollient enemas, and a proper regimen, which will commonly include the use of stimulants in moderate quantity together with a nourishing liquid diet.

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[1] Op. cit., p. 402.

HEPATITIS is rather rare as a complication of remittent fever, although the liver is usually enlarged from congestion in the early stages of the disease. In 138 cases among European officers treated in the European General Hospital at Bombay, this complication was noted in 7 cases, of whom 5 recovered. In 114 cases in natives, hepatitis was present in 3 (Morehead).

JAUNDICE is a more frequent complication. Woodward says that during the late war "jaundice was most prevalent among those armies exposed to the most intense malarial influences, as indicated by the prevalence of malarial fevers; but its monthly fluctuations did not in any way correspond with those of the latter affections, and, contrary to what might have been anticipated, in view of the relation believed to exist between an elevated temperature and hepatic disorder, it was most common in the winter and spring months and rarest in the summer."[1]

In 114 selected clinical cases among natives in Bombay jaundice was present in 28, and 10 of these proved fatal. In 90 fatal cases among European officers this complication was present in 7. According to Morehead, jaundice seldom comes on before the fifth day, and is almost invariably attended with tenderness below the margins of the seventh, eighth, and ninth right ribs. This author, while admitting that the pathology of this complication is not well understood, thinks it probable that its most important relation is to inflammation of the mucous membrane of the duodenum. Traces of inflammation of the mucous membrane of the duodenum and stomach were observed in 6 of the 10 fatal cases above referred to. This view of the pathology is said to be supported by the fact that the symptoms are "sure to be aggravated by the injudicious use of calomel and purgatives."

Woodward believes that hepatic congestion and suppression of the biliary secretion is the cause of epidemic jaundice as it occurred in our armies during the war, and remarks that "in the malarial regions in which it has occurred, deficient hepatic secretion is a characteristic phenomenon; carried to a high degree this deficiency produces the form of jaundice under discussion."[2]

The old idea that "biliousness" calls for the administration of mercury no doubt still controls the treatment of cases of remittent fever complicated with jaundice in some parts of our own country as well as in India. It is hardly necessary to remark that in any view of the pathology of this complication, mercurial treatment is left without any theoretical support, since it has been shown that it does not increase the biliary secretion. Nor do we know of any satisfactory clinical evidence of its special value in the treatment of jaundice, which, according to Dr. Flint, should in a majority of cases be addressed to a subacute inflammation of the stomach and duodenum.

Laxatives or cathartics are only required for the relief of constipation. And, when required, the mildest forms are to be preferred. There is no ground for the supposition that mercury exerts any special efficacy, but a few grains of calomel or blue mass frequently prove as mild and effective as any form of cathartic or laxative, followed, if necessary, by a saline draught. The latter alone will often suffice. The saline mineral waters, such as the Congress or Kissingen water, will frequently secure an adequate laxative effect. Remedies to soothe the inflamed mucous membrane are useful, such as small doses of morphia, or some of the succedanea of opium, viz., belladonna, hyoscyamus, conium, etc. Conium has been considered as a remedy having a special efficacy in jaundice. Its apparent efficacy may be accounted for, in part, by its usefulness as a soothing remedy, and partly by its supplanting active cathartics and emetics which are injurious.[1]

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[1] Camp Diseases, p. 194.

[2] Ibid., p. 201.

Such is the treatment of this complication, as given by one of our most accomplished clinical teachers. But our attention must not be drawn from the main object of treatment, which is to arrest the progress of the remittent fever. In view of the gastro-duodenitis it will generally be advisable to give quinine for this purpose by enema or by hypodermic injection.

The following case is reported by Morehead:

Remittent Fever with Jaundice—Tenderness at the Margin of the Right Ribs—Death from Exhaustion—Enlargement and Biliary Congestion of the Liver—Gastro-duodenitis—Hepatic Cells Distinct.—Sutwa P——, a Hindu rope-maker, twenty-seven years of age, and stout habit of body, after suffering for twelve days from febrile symptoms, without, as reported, distinct remissions, was admitted into hospital August 7, 1849. The abdomen was full, without induration, but with tenderness at the margin of the right ribs. He had occasional vomiting, and the tongue was coated. The bowels were reported to be regular. He admitted that he made occasional use of spirits. Thirty-six leeches were applied to the epigastrium; quinine in four-grain doses, with blue pill and ipecacuanha, was given during the remission. There was not much heat of skin on the 9th and 10th; the pain was relieved and the vomiting had ceased. *Some compound powder of jalap was given on the 10th. On that evening there was a febrile exacerbation*, which was continued on the 11th (there having been shivering at midnight), with increase of tenderness at the epigastrium and margin of right ribs, dulness to within an inch and a half of the umbilicus, and commencing jaundice. Respiration short and hurried, pulse frequent and small, and tongue dry, with dark fur. *Fifty leeches were applied to the margin of the ribs, and ten grains of calomel*, with four of compound extract of colocynth, were given. *At noon the skin was cool, the pulse feeble*, and one pale evacuation had passed. The side was said to be easier, but the breathing continued hurried *and he died* about an hour after the report. [Italics by present writer.]

Dr. Morehead makes the following remarks:

In this case the fatal result was expedited by the injudicious use of depressants in the advanced state of the fever; indeed, it is not improbable that the exacerbation on the 10th was favored by the purgative then given.

Inspection Three Hours after Death.—The body was not much reduced, and the tissues were tinged deeply yellow. *Chest:* The lungs were crepitating, but somewhat inflated. There were no adhesions between the pulmonary and costal pleuræ. The heart was healthy. *Abdomen:* The liver was much enlarged and reached beyond the margin of the false ribs, from the tenth rib of the right side to within an inch and a half of the umbilicus, and thence to the most prominent part of the seventh left rib. No adhesions existed between it and the surrounding parts. When incised, the surfaces were of a mixed red and olive-green tint, and the substance was softer than natural throughout. The gall-bladder contained serous-looking bile. The stomach was full of half-digested food, and its mucous membrane was of a uniform rose color, except in a few places where there was a deeper dotted redness with some degree of softening. The inner surface of the duodenum was tinged with bile, and its mucous membrane, as well as that of the large intestine, was of a redder color than natural. The kidneys were large and of a dark (almost black) red color throughout, evidently from congestion of blood. The spleen was not enlarged. The head was not examined. A small portion of the glandular substance of the liver was examined under the microscope and exhibited the hepatic cells distinct.

PAROTIDITIS ending in suppuration is an occasional complication of remittent fever. Dr. Morehead has observed it only in natives, and always associated with febrile symptoms of a marked adynamic character. The following case is reported by Fayrer (op. cit.):

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[1] Flint's Practice of Medicine, p. 548.

Malarial Fever and Parotiditis.—Sepoy of Sixteenth Native Infantry, aged twenty-three, was admitted into hospital at Dacca, under Dr. Wise, on April 15, 1873, with remittent fever, assuming a very violent form on 17th. After vomiting he became insensible, and partially recovering consciousness, was found to be hemiplegic on left side. On May 4th, the twentieth day of illness, a hard swelling over right parotid gland appeared. On the 10th it opened. By the 27th it had healed. On June 11th muscular power in limbs was nearly equal and his mental faculties were unimpaired. Left on this date for nine months' leave (particulars given by Surgeon J. Duke).

PNEUMONIA comes, perhaps, next to dysentery as a cause of mortality among the victims of malarial poisoning. But, like dysentery, it is rather by attacking those subject to malarial cachexia than as a complication of remittent fever that it becomes an important factor in increasing the mortality in malarious regions. The pyrexia in these cases of pneumonia in malarial subjects, as in other febrile affections in such individuals, has a remittent or intermittent character. This has given rise to the supposition that the pneumonia in these cases is of malarial origin. There is, however, no ground for this belief, any more than for the supposition that in India malaria may produce cholera, in the West Indies yellow fever, in certain tropical regions dysentery, and in our own Northern cities a continued fever lasting three weeks or longer and not curable by quinine.

This so-called malarial pneumonia is unknown in certain regions where malarial fevers of the most typical and intense form are extremely prevalent, and in those regions where it does prevail, it is not so much during the season of remittent fevers as later, when malaria is no longer evolved so abundantly, that pneumonia occurs by preference among those subject to malarial cachexia or to debility from some other cause. As large numbers of individuals are often exposed simultaneously to the causes which produce pneumonia—sudden changes of temperature, in combination, perhaps, with a special cause (?)—a veritable endemo-epidemic sometimes occurs in regions where malarial diseases were extremely prevalent earlier in the season. The same climatic changes which induce pneumonia in some of the victims of chronic malarial toxæmia may cause a return of ague or an attack of remittent fever in others, and pneumonia may in this case appear later as a secondary affection or complication of the malarial disease. The malarial element, or rather the fact that the vital resistance of these cachectic individuals is greatly reduced by the effects of malaria, gives to these cases a gravity comparable with that of pneumonia in scorbutic subjects, or the victims of crowd-poisoning or of chronic alcoholism.

Colin remarks with reference to the etiology of this so-called "malarial pneumonia:"

That these pulmonary accidents differ from the acute manifestations of malarial intoxication [in etiology] is proved by the fact that they occur in Rome, as in Algeria and in La Bresse, not during the reign of the annual epidemic, nor at the epoch of simple and pernicious intermittent fevers, but in winter, at the moment when the soil seems to have become completely inoffensive; and they explain the enormous mortality of this season. These accidents occur in malarial regions, nearly every year, with much greater regularity in their return than our simple pneumonia ("*pneumonie franche*"); they coincide with the reduction of temperature during the winter months, and present relapses, often of a most frightful character, under the influence of the north wind.

As in pneumonia in scorbutic and alcoholic subjects, these cases in malarial cachectics are remarkable by the slight intensity of the initial chill and of the pain. The expectoration is less viscous than in ordinary pneumonia, and the crepitant râle is less dry. The reaction is so feeble that often dyspnœa and a hectic flush of the cheeks are the first phenomena which attract the attention of the physician; as in scorbutus and chronic alcoholism, the pneumonia is frequently double. . . . By its gravity, also, the pneumonia of these cachectic persons approaches that of drunkards and of scorbutic subjects. . . . Out of six cases in persons suffering from malarial cachexia, who were admitted to hospital in November and December, 1865 (in Rome), the mortality was one-half, an enormous figure when we consider the habitual benignity of pneumonia in our army. . . . In the same year (1865) we had the opportunity to verify the fact that frank pneumonia is as benign in this city as in our garrisons in France. During the preceding spring, at the epoch when there had been no malaria for three months, and when every one had recovered the normal attributes of health, a little epidemic of pneumonia sent thirty-six cases to the hospital. The disease was of a frank character, and identical in its evolution with pneumonia as seen in France. Thanks to the mildness of the climate, convalescence was even more rapid than in France, and out of thirty-six cases only two proved fatal. Thus in the same hospital, among men of the same age and nationality, the mortality varied, according as they had or had not cachexia, from five to fifty per cent.

The *treatment* of pneumonia when it occurs as a complication of remittent fever, or as a primary disease in one suffering from malarial cachexia, consists in the liberal use of quinine, concentrated nourishment, and alcohol. In short, the object in view from the first must be to support the patient's strength by food and stimulants, and to neutralize the malarial element in the case by the administration of quinine, trusting to nature for the cure of the pneumonia.

CHAPTER X.

HEMORRHAGIC MALARIAL FEVER.

In the ordinary forms of malarial fever—intermittent or remittent—even when the intense action of the malarial poison is manifested by the phenomena designated "pernicious," hemorrhage is an extremely rare event, and when it does occur—epistaxis, for example—may be considered accidental. Yellow fever, on the other hand, is eminently a hemorrhagic fever, and few fatal cases occur without a manifestation of this tendency to passive hemorrhages from the mucous membranes, and especially from the stomach—black vomit. This is generally recognized as one of the most important distinguishing characters of the two diseases.

Nevertheless, cases of malarial fever attended with hemorrhage occasionally occur in all parts of the world where malarial diseases prevail. We have already referred to the fact that passive hemorrhages—usually from the gums, the nostrils, or the bowels—occasionally occur in cases of remittent fever in which the patient has fallen into a typhoid condition—"adynamic remittent fever"—either as a result of a scorbutic or septic complication or in consequence of the intensity and duration of the malarial disease. But this symptom is not sufficiently constant or prominent to give character to the disease and justify the use of the term hemorrhagic as applied to these cases. There is, however, a form of malarial fever in which hemorrhage from the kidneys is a constant symptom. This is the disease known in our Southern States as "hemorrhagic malarial fever," and in other parts of the world under a variety of names which express its hemorrhagic character, and some of which indicate the source of the hemorrhage—*e.g.*, malarial hæmaturia, fièvre bilieuse mélanurique, etc.

It may be that cases of malarial hæmaturia, whether of mild or severe type—intermittent, remittent, or continued—would be more properly included under the heading "complicated malarial fever." But inasmuch as the nature of the complication is not definitely known, and as the term hemorrhagic simply expresses a clinical fact and does not commit us to any theory as to the cause of the hæmaturia, there can be no objection to the designation which does not apply with equal force to the other clinical varieties of malarial fever which we have described separately—*e.g.*, pernicious intermittent and remittent fever, ardent malarial fever, etc.

Intermittent Hæmaturia.

Definition.—This affection is characterized by the occasional, and generally periodic, discharge of albuminous urine, more or less deeply tinged with the coloring matter of the blood and frequently containing red blood-corpuscles and casts of the uriniferous tubules. It occurs most frequently in malarious regions, and in individuals who have suffered repeated attacks of malarial fever; and the discharge of bloody urine is often—but not always—attended with the symptoms which characterize an attack of ague, and with jaundice.

SYNONYMS.—Malarial hæmaturia; paroxysmal hæmaturia; hæmatinuria.

It is hardly probable that this is a new disease, although but few references to it are to be found in medical literature prior to the valuable report made by Dr. George Harley in 1865.[1] Since this time English and American periodicals have from time to time contained reports of cases, and the contributions from physicians in the Southern portions of the United States show that the disease in question is not infrequently encountered in the malarious sections of this country. We learn from a recent paper by Professor Tyson,[2] of Philadelphia, that it is by no means rare even as far north as the State of Pennsylvania. This is not surprising in view of the fact that cases occur in England and even in Scotland.

Copeland says in his "Dictionary of Practical Medicine:"

> Periodic hæmaturia is not uncommon in miasmatic climates, and it is, although rarely, even seen in this country [Great Britain] among those who have been exposed to malaria, or have resided long in warm climates, or suffered from periodic fevers.

Among the earlier references to this affection we may mention the following: Dr. Elliotson[3] (1832) refers to a case of ague in which a discharge of bloody urine occurred during the cold fit.

In the *London Medical Gazette* of January 19, 1849, Dr. R. B. Todd says:

> A state of general cachexia, such as often occurs in scurvy, may bring on hæmaturia, or such as results from an aguish state brought on by the malaria of marshy districts.

In this country Dr. Charles Lee, in 1860, refers to the frequent occurrence of hæmaturia in the Southern States, in connection with derangements of the liver and spleen (McDaniel).

Since the termination of the civil war, numerous cases of intermittent hæmaturia have been reported, and the grave form of malarial hæmaturia attended with jaundice, which is commonly known in this country as "hemorrhagic malarial fever," and which we shall describe separately, has received very considerable attention in our periodical medical literature.

ETIOLOGY.—Intermittent hæmaturia is generally recognized as being of malarial origin, and in a large majority of the cases there is a history of exposure to malarial influences and of previous attacks of intermittent or remittent fever. But the malarial origin is not always very apparent, and the attack is, perhaps, more often immediately due to exposure to cold, and especially to getting wet, than to the direct influence of the malarial poison. Indeed, we have a vast amount of negative evidence in favor of the view that malaria *per se* is not competent to produce this form of disease; and it seems necessary to assume the existence of a special cooperating cause, or to admit that some organic change in the structure of the kidney or in its nerves is responsible for the hæmaturia. In some instances the discharge of bloody urine is attended with the symptoms—more or less well defined—of an attack of ague; but this is not always the case, and sometimes we have only the periodic recurrence of the bloody discharges and the malarial history of the individual upon which to found the hypothesis that the disease is due to the action of malaria. This evidence is not, according to our view, entirely convincing, for while it is beyond question that malarial subjects are most liable to intermittent hæmaturia, it does not follow that this is due to the direct action of the malarial poison. It is well known that intercurrent affections in malarial subjects very commonly have an intermittent character, although the pathological condition upon which the morbid phenomena depend may have an independent origin—as, for example, in dysentery or pneumonia in malarial subjects. On the other hand, periodic phenomena—physiological or morbid—may occur quite independently of the action of malaria. As examples we may mention the periodic recurrence in the evening of the intolerable itching and burning of chilblains, and periodic morning priapism due to a distended bladder. But inasmuch as it has not been shown that paroxysmal hæmaturia may occur quite independently of the action of malaria—as is true in regard to dysentery, pneumonia, and other diseases which have been improperly called malarial—we admit the probability that there is no independent specific cause concerned in the etiology of this affection; and whatever may be the pathological condition which favors the bloody discharges, it is probable that they would not occur independently of the malarial influence. But the fact that they only occur, under the influence of this cause, in exceptional cases indicates that conditions relating to the individual are also essential. The exact nature of these conditions is unknown, but they probably relate to organic changes in the kidneys, and depend upon some cause more active in men than in women; for the reported cases have almost invariably been in males. According to Bérenger Féraud, persons of intemperate habits are especially subject to the grave form of malarial hæmaturia—hemorrhagic malarial fever—and the possibility suggests itself that the same cause may also give rise to a predisposition—based upon structural changes or functional debility—to the form of hæmaturia at present under consideration.

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[1] Intermittent Hæmaturia: Medico-Chirurg. Trans., London, 1865.

[2] James Tyson, M.D.: Malarial Hæmaturia, The Medical News, Phila., May 12, 1883.

[3] London Lancet, 1832, p. 500.

Symptoms and Course of the Disease.—The bloody urine may appear during a paroxysm of intermittent fever which has been preceded by one or more paroxysms unaccompanied by this symptom, or it may appear suddenly in one who has been subject to malarial attacks but has not experienced one for some time. In this case it is commonly induced by exposure to damp and cold. After such exposure the patient gets up in the morning feeling languid and indisposed to take food or to exert himself. Later he may have slight chilly sensations or a distinct chill followed by more or less fever, and he discovers that his urine, which was perfectly clear when he first got up, has suddenly assumed a bright or dark red color, or it may be of the color of porter. Upon standing it deposits a copious reddish-brown sediment. Two or three discharges of this character may take place and then the urine suddenly or gradually assumes its normal appearance. The discharge of bloody urine is sometimes preceded by a sense of fulness, or of pain, in the region of the kidneys; and this, with a feeling of weariness, may be the only symptoms attending the attack other than the hæmaturia. The periodic character is manifested by a recurrence of the attack every day, or every second day, at the same hour. Or the paroxysms may occur at longer intervals and without any very decided regularity as to the date of recurrence. In protracted cases this seems often to depend more upon accidental causes than upon a distinctly periodic tendency, and in these cases the slightest exposure to cold will often induce a return of the bloody discharges. Hæmaturia is often rather continued than intermittent in these chronic cases. Dr. Tyson, while admitting that the disease is malarial and that a majority of the cases have an intermittent character, says that only two out of the seven cases which have come under his observation were distinctly intermittent. He says:

> I prefer the term malarial to intermittent or paroxysmal, not only because it more precisely indicates the cause of the condition, but also because the condition itself is by no means always intermittent, but sometimes continues without interruption until checked by appropriate treatment, and I have known it to continue uninterruptedly for a year, notwithstanding all treatment.

The victims of malarial hæmaturia have a cachectic appearance and jaundice is an occasional symptom. In an interesting case reported by Druitt,[1] the patient, prior to the appearance of blood in his urine, was repeatedly told by his friends that his face was of a "singular dusky, earthy color."

CONDITION OF THE URINE.—In the case just referred to, reported by Druitt, in which repeated attacks occurred during a period of six years, the most careful examination failed to disclose anything abnormal in the character of the urine during the intervals when it was free from blood.

> One morning, at ten, at a seaside place, the urine was pronounced perfectly healthy by an eminent chemist; at 1 P.M. it was dark bloody, just of the color and appearance of water in which raw meat has been macerated; in the evening it was again natural.

During the paroxysmal attacks of hæmaturia the urine varies in color, according to the amount of blood-pigment present in it, from a "smoky hue" to a deep claret, or is even darker than this, being sometimes the color of porter. It is usually acid and always albuminous. The specific gravity varies greatly and may be as high as 1028. The reddish-brown sediment which is deposited in abundance is said by Tyson to be made up chiefly of blood-disks and of the granular débris resulting from their disintegration. Sometimes, however, a careful microscopic examination fails to reveal the presence of red blood-corpuscles, which are very quickly disorganized when the urine becomes alkaline, while in an acid fluid they may preserve their form although they speedily loose their color. Dr. Tyson has been able to verify the presence of colorless blood-corpuscles in specimens of urine in which no red blood-disks were to be found, but in which spectrum analysis and the production of Teichmann's hæmin crystals proved the presence of blood pigment. Tube-casts made up of granular matter and red corpuscles are often present in the urine, and hyaline casts may also be found in some instances. Analyses made by Drs. Moore, Letheby, and Harley show that there is a deficiency of urea in the urine passed during the paroxysm.

In Dr. Druitt's case, above referred to:

> There appeared to be a diurnal paroxysm of coldness, depression, and prostration—sometimes seeming to be brought on by the act of getting out of bed (for on assuming the upright position one leg would go numb and chilly), sometimes by the act of exposing the skin to the air or by washing in cold water. Sometimes when, by way of experiment, the patient remained in bed, the feet and hands would become a little cold, wet, and blue about 9.30 A.M.; but he never, as a rule, had any bloody urine so long as he remained in bed.

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[1] Robert Druitt, M.R.C.P.: Med. Times & Gaz., April 19, 1873.

To resume. The morning paroxysmal elimination from the kidneys might be (1) a small quantity of highly albuminous urine, so filled with epithelial casts from the kidneys as to look like jelly or white of egg (this by itself was rare, and only happened during the first year of the malady); (2) there might be a prodigious excretion of red, yellow, and pink coloring matter (and this was the most constant diurnal symptom, appearing in the urine secreted between 10 A.M. and 4 P.M.); (3) there might be blood which presented three varieties of appearance.

The commonest and slightest appearance of blood was as a dark brown-black or chocolate sediment, either alone or mixed with jelly-like kidney epithelium, or with the pink and red colored sediment, or both; whilst the supernatant urine would not be much darker or bloodier-looking than natural. This sediment was originally pronounced by Dr. Beale to be a mass of amorphous blood-stuff—disintegrated blood-globules moulded in the kidney tubes; and his opinion was that the malady was not a hemorrhage in the proper sense of the word—*i.e.*, although a loss of blood-*substance*, yet not of substance having the form and organization of blood. Blood-*globules*—of natural shape—are most rarely seen in this, whilst in other forms of hæmaturia they abound. Whilst the blood is excreted in this form so as to look like an occasional sediment of chocolate, the disease might easily pass unnoticed by observers who are not specially on the look-out.

The second and commonest form in which the blood presented itself was that of *dark* grumous matter. with an abundant sediment like the last, of amorphous and disintegrated blood-globules in the form of casts, but with the greater part of it dissolved in the urine, the supernatant part of which was deeply colored.

In the last form, which was rare, and occurred only about a dozen times in half a dozen years, the patient was seized after breakfast with a sudden irresistible desire to pass water, which was intensely irritating, slightly alkaline, and of the brightest arterial scarlet.[1]

DIAGNOSIS.—The periodic recurrence of the bloody discharges in this affection is generally admitted to be evidence of its malarial origin, and distinguishes it from hæmaturia from other causes—*e. g.*, cancer, calculus, scorbutus, etc. The presence of tube-casts made up of blood-corpuscles shows that the blood comes from the kidneys. When the urine is simply tinged with the coloring matter of the blood—hæmatinuria or hæmaglobinuria—and does not contain blood-globules, we may be sure that the bloody discharge is from the kidneys and not from the bladder or ureters. The absence of vesical irritation and of clots will also be evidence that hemorrhage is renal rather than vesical. When there is any doubt with reference to the hæmic origin of the pigment to which the color of the urine is due, this may be settled by spectrum analysis or by the production of Teichmann's hæmic crystals.[2]

PATHOLOGY.—Nothing definite is known as regards the pathological condition upon which intermittent hæmaturia depends. Some have supposed that it relates rather to the blood than to the kidneys, and that disorganization of the corpuscles occurs as a direct result of the action of malaria, the hæmatinuria being due simply to excretion by the kidneys of the products of this disorganization. But we have no evidence that there is a greater destruction of red corpuscles in these cases than occurs in severe cases of intermittent or remittent fever unattended by this phenomenon; and the explanation will not cover the cases in which blood-corpuscles and tube-casts made up of red blood-disks are found in the urine. It is evident that in a certain proportion of the cases, at least, the bloody urine is due to passive renal hemorrhage, and it seems altogether probable that the destruction of corpuscles occurs in the kidneys themselves when we have hæmoglobinuria independently of the presence of blood-corpuscles in the urine.

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[1] Loc. cit , p. 410.

[2] Place a drop of the sediment upon a glass slide and allow it to dry. Mix thoroughly with a few particles of common salt, and cover with a thin glass cover, under which allow two or three drops of glacial acetic acid to pass. Carefully warm the slide for a few seconds over a spirit-lamp, and when most of the acetic acid is evaporated examine by the microscope. Hæmin crystals will be seen to crystallize out as the mixture cools (Professor Tyson, in the Med. News, loc. cit.).

The kidneys are doubtless hyperæmic when the bloody discharge occurs, but it is difficult to believe that intermittent hyperæmia, due to the paralyzing action of the malarial poison upon the vaso-motor nerves, is a sufficient explanation of the phenomenon in question; and it seems altogether probable that this is associated with some structural lesion or chronic organic disease of the kidneys.

Ponfick goes so far as to say that the exudation of hæmoglobulin is not possible without the occurrence of marked diffuse nephritis. Recently Lebedeff has sought to investigate the more minute alterations of the kidney in hæmoglobin exudation, but without very definite results. These, however, on the whole, seem to confirm Ponfick's view as to the presence of an inflammatory process.[1]

PROGNOSIS.—Intermittent hæmaturia is not fatal *per se*, but the reported cases show that the morbid condition upon which this symptom—for we cannot properly speak of hæmaturia as a disease—depends is often very persistent, and that the bloody urinary discharges may occur at intervals for months, and even for years, in spite of the most diverse measures of treatment.

TREATMENT.—Authors generally agree that quinine is the most important remedy in these cases; but, as in other chronic affections due directly or indirectly to malaria, quinine is often only of temporary benefit and fails to effect a permanent cure. The patient is relieved for a time, but relapses constantly occur as a result of exposure to cold or some other exciting cause, often of the most trifling nature. Professor Tyson says: "The treatment is distinctly that of malarial disease, and I have seldom seen more brilliant and satisfactory results than have followed the use of quinine in a case accurately determined, although such results are not invariable, and I have known the disease to resist for a long time the most thorough and judicious use of anti malarial remedies." In Dr. Druitt's case, heretofore referred to, very small doses of quinine were tried at first without evident benefit, and the patient, who was himself a physician, rejected the remedy and resorted to the use of repeated small doses of calomel or blue pill with colocynth, and by the advice of medical friends persisted in the use of these remedies, although he received no benefit from them and found that "calomel in the dose of one grain, so far from acting as a cholagogue, really shut up the bile, but brought away profuse colorless discharges of mucus, very much to the patient's detriment." If there was constipation purgatives made the patient more comfortable, but otherwise they were injurious or useless. The preparations of iron never did the slightest good and always caused dyspepsia and headache.

Astringents of all sorts were taken from time to time—tannin, gallic acid, tincture of galls, sulphate of zinc, alum mixed with ginger (a popular remedy for ague), oil of turpentine in ten-minim doses, ether, mineral acids, liquor potassæ, the oil and extract of the eucalyptus globulus, magnesia, Vichy water, the waters of Vals, ergot in full doses—these were all of no use. It would be almost useless to recapitulate all that the patient tried; but of those already mentioned turpentine was the best.

Finally, after suffering for months the patient ventured to take an eight-grain dose of quinine, and "felt more benefit in one hour than he had done from anything he had taken during the foregoing year and a half." Dr. Druitt says, in referring to the treatment of this case: "Of medicines deserving the name there was but one, and that was *quinine* in full doses." But notwithstanding the benefit derived from the use of this remedy, it did not cure the condition upon which the hæmaturia depended, and constant relapses occurred, as shown by the following interesting statement:

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[1] Quoted from Professor Tyson's paper, previously referred to.

> The quinine was continued in eight-grain doses in the morning and four in the afternoon for ten days, and then was gradually dropped; and for twenty-one days the malady seemed suppressed, and the patient thought himself quite well; but on April 16th it came back. Then it was staved off again by fresh doses and larger doses. Since then the patient has taken quinine immensely, and the following is a summary of its effects: As for the daily periodic attacks of depression followed by hæmaturia, at first, as we have seen, it banished them for twenty-one days. When resumed after a relapse in one full morning dose of eight to ten grains, it again put an end to the attacks for a time. But as time went on it was clear that the quinine acted as a temporary and palliative, not as a radical remedy; for if it were left off in bad weather and if there were any unusual exposure to cold, the coldness of the feet and bloody urine would follow. Secondly, to take quinine in large doses soon becomes incompatible with the occupations of life. The ringing in the ears which accompanies cinchonism is indicative of a state of the brain—a kind of mild exhilaration—fit for little besides novel-reading or other amusement. Thirdly, it became painfully clear that the quinine gradually lost its effect in preventing the hæmaturia, and that no perseverance with it or accumulation of it in the system sufficed to eradicate the disease. The patient was in the habit of taking a cup of coffee before rising, and with this he used to help himself to quinine powder out of a bottle, and to bolt down ten to twenty grains wrapped up in moistened wafer paper, the use of which he was taught by Mr. Squire. The best effect of quinine was when it was resumed in a full morning dose after having been discontinued for some days. In the last and severest feverish attack in July, 1871, Sir William Gull pulled him up at once out of it by very large doses of quinine, combined with salicine and the liquid extract of bark; and any subsequent feverish attack has always been suppressed by the same remedies. With regard to the hæmaturia, the quinine has certainly been of enormous service in keeping it at bay; but its virtues have become gradually less and less, and often fail altogether. Nevertheless the patient always feels the better for it, and could not have lived all this time without it (loc. cit.).

Dr. Tyson has found that cases which resist the use of quinine alone will sometimes yield to this remedy after the administration of a mercurial cathartic—ten grains of calomel followed by a saline cathartic. In the case of a negro who had malarial hæmoglobinuria, thirty-six grains of quinine failed to break the attack, but the same quantity given after ten grains of calomel had acted succeeded. In this author's experience those cases in which quinine fails to effect a cure are not benefited by the administration of arsenic pushed to the fullest extent admissible, or of arsenic and iron; nor has he found ergot to be of any special value in the arrest of the renal hemorrhage. The administration of mineral and vegetable astringents is recommended—vegetable acids, persulphate of iron, acetate of lead, alum, gallic acid, catechu, kino, etc.—but it is evident from the utter failure of these remedies in Dr. Druitt's case, and from the intractable character of the malady in cases coming under Dr. Tyson's own care, that the treatment by astringents is not very successful, and the propriety of administering styptics by the mouth for the relief of renal hemorrhage is, perhaps, questionable. Rest is undoubtedly an extremely important part of the treatment; and among the remedies found really of service in Druitt's case *warmth* is placed in the front rank.

> It seemed as though the whole phenomena, of which the bloody urine was the climax, were suppressed when the patient was made warm early in the day, and kept so. He never had bloody urine when feverish, though the excretion of lithates and

pink stuff was great, nor yet if he remained in bed, which he did once or twice till evening, in cold weather, by way of experiment, and a few times for influenza or other accidental indisposition. An ordinary warm bath, or warm hip-bath with a steaming blanket, as recommended by Dr. Stokes, was sometimes efficacious as a preventive. . . . But the most useful and comforting means of making the surface warm and keeping it so was the mustard bath.

Cases.—The following case is reported by Professor Tyson (loc. cit.):

The patient was a lawyer, who consulted me in June, 1881, at the suggestion of Dr. W. W. Covington, of North Carolina He had frequently had "chills," and a congestive chill in 1873. Three months before I saw him he began to pass bloody urine. He had no other symptoms, except a soreness and weakness in the neighborhood of the sacrum, extending into the outer part of the left thigh. The urine passed for me at the time of his visit was a dark reddish-brown in color, acid in reaction, had a specific gravity of 1028, and deposited a sediment of almost tarry consistence, which was made up almost entirely of blood-corpuscles, and was, of course, highly albuminous. There were no tube-casts. He had been a dyspeptic since seventeen years of age, and medicines disagreed with him; but he was treated faithfully with quinine, iron, arsenic, ergot, benzoate of lime, all without the slightest effect. At the end of about a year from the time he consulted me, he heard of the Jackson Spring, located in Moore County, N. C., fifteen miles distant from Manly Station, on the Raleigh and Augusta Railroad. He went there and remained one week. He states that for the first two or three days the water acted decidedly on his kidneys, and he voided a number of clots of blood. *On the third day all traces of blood disappeared*, and it recurred but once since, on a very cold day in November last, but again disappeared after a day or two in the house. This statement is so direct, and my patient is so intelligent and reliable, that I could not but be impressed by it, and I am quite anxious to repeat the remedy in another case. Unfortunately no precise analysis of this water seems to have been made; but from what my friend writes it evidently contains iron and sulphur, and magnesia is also said to be present. It is promptly diuretic.

The favorable result in this case makes it seem worth while to call attention to this spring; at the same time we suggest the possibility that the amount of water drunk at these mineral springs may perhaps in certain cases be the important point rather than the character of the mineral ingredients present. Dr. J. E. Thompson, of Missouri, in a paper contributed to the *St. Louis Courier of Medicine* (April, 1881), says: "Free diuresis is desirable; but this is best produced by the free use of water, and not by the use of irritating diuretics, such as turpentine, etc. . . . Water, plain or combined with mucilaginous substances, is the only diuretic I have had occasion to use in treating a great number of cases during a service of four years as Confederate surgeon and a ten-years' residence in the malarial districts of White and Arkansas Rivers, in Arkansas. Cure the malarial malady and you can cure the hæmaturia. . . . I regard quinine as the sheet-anchor in the treatment of malarial hæmaturia."

The following case is reported by Druitt:[1]

Mr. ——, aged fifty-six years, tall and sallow, was sent to me by Sir James Paget on December 28, 1869. He passed several years in India, during which he had a severe liver attack and piles, which were successfully treated. He also had an attack of malarious fever. Still his health was good on the whole till the year 1859, when, during a long ride in winter, he got excessively chilled, and on making water on his return passed what seemed to be "black blood." Ever since that he has been subject from time to time—say once in three or four months—if he gets chilled, to an attack of fever and ague, followed by sweating; and as these attacks go off he passes "black water," with a mental sense of relief, as if the black water carried off something noxious. These fever and ague attacks occur, as has been said, seldom, and are only brought on by imprudent exposure ; but at any time during cold weather and northeast winds he is liable to rise in the morning feeling very seedy, and although the urine is all right then, that which is passed after breakfast, and sometimes after lunch too, is as thick and black as tar. Then the urine passed during the evening and night is quite clear and natural. At the time of these attacks a peculiar sallowness across the forehead is noticed by the patient's family. He is conscious that the morning is the weak part of his day. Formerly headache, now a kind of cold nausea, accompanies the paroxysms. If he gets up well, and keeps warm, and takes exercise, he may be all right ; but if he drives out in a northeast wind he is very liable to an attack. He also believes that cold water drank incautiously has brought it on. He can bear to wash the face with cold water, but not the hands.

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[1] Robert Druitt, M.R.C.P., in Med. Times & Gaz., Lond., May 10, 1873.

The patient is tall, sallowish, and has lost weight ; he sleeps well and warmly ; has no giddiness, nor numbness, nor inequality of circulation and warmth. The tongue is reddish and fissured ; the appetite good, no thirst nor dyspepsia ; bowels torpid ; the pulse is 60, steady. There is no local blueness or cramp ; the effect of cold is general shiverings, not local stagnation ; he perspires freely in warm weather ; the urine is very often of a dark orange color, with red sediment, but the morning urine is generally natural. He never had actual gout. The hæmaturic attacks leave a little uneasiness and sense of weakness in the loins, but not enough to notice seriously. . . . The urine passed during the paroxysms was in all respects like that noticed as the second variety of the preceding case—dark ; a copious grumous sediment, full of disorganized blood-globules moulded into casts, with the supernatant urine deeply tinged with blood.

There were two remedies which I prescribed, and which did him good. One was the mustard-bath used freely in the morning, to get up a good cutaneous circulation ; and the other quinine in large doses—*i.e.*, fifteen grains daily (ten grains early in the day and five later). By means of these he considered himself virtually cured, so far that he could live in England and keep his malady at bay. Instead of hanging about him for days together, it came on only once in six or eight weeks, after exposure or imprudence.

Grave Malarial Hæmaturia ("*Hemorrhagic Malarial Fever*").

Definition.—A fatal form of malarial fever prevailing only in intensely malarious regions—chiefly in the tropics—and characterized by jaundice and hæmaturia, or hæmatinuria. The pyrexia may be either intermittent, remittent, or continuous in character. Those attacked are for the most part the victims of chronic malarial cachexia or of chronic alcoholism.

Synonyms.—Hemorrhagic paludal fever ; icterode pernicious fever ; bilious hæmaturic fever ; bilious fever of the tropics ; malignant malarial hæmaturia ; country yellow fever ; black jaundice ; malignant jaundice ; bloody chills ; yellow chills, etc. *Fr.*, *fièvre bilieuse mélanurique ; fièvre bilieuse hématurique ; fièvre pernicieuse ictérique ; fièvre jaune palustre; fièvre jaune des créoles et des acclimatés*, etc.

Etiology.—The hemorrhagic malarial fever at present under consideration is due to the recent and intense action of malaria, and does not occur as a remote result of malarial poisoning, as is the case in the form of intermittent hæmaturia previously considered. It is therefore unknown outside of malarious regions, except, possibly, in persons who have very recently come from such regions.

Like other forms of malarial fever, it is endemic only where the conditions of climate and soil are favorable for the generation of malaria, and like them it never prevails as a veritable epidemic. The area of its endemic prevalence is more restricted than that of malarial diseases generally, and corresponds with the territorial limits which are recognized as especially prolific in malaria.

Such regions are found in tropical America, in the East and West Indies, upon the coast of Africa—and doubtless in the interior also—and in the Southern portions of our own country, especially in the rich river bottoms, and in swampy localities in the States of Alabama, Mississippi, Louisiana, and Arkansas.

In the Northern portions of the United States the disease under consideration is practically unknown, and it was so rare in the Southern States mentioned prior to the late war, and has since become so common in certain localities, that some physicians have been disposed to regard it as a new disease. There is evidence, however, that cases occurred long prior to the war, and the increased prevalence since is probably due to causes connected with this protracted struggle—causes relating both to malaria-production and to the susceptibility of the exposed population.

That the disease is not new in this country seems to be established by the evidence given by Dr. McDaniel, of Camden, Ala., to whom we are indebted for several valuable papers relating to it. He says:

> In calling up my own reminiscences, I am sure that I have occasionally, ever since my boyhood, seen isolated cases of what was considered intense bilious fever, with the surfaces and under tissues stained deeply yellow and with the urine deep red. They were nearly all fatal, and were called in older phrase "bilious congestive," and in more recent "pernicious bilious." I have also, but more rarely, known groups of similar cases associated; say three or four cases occurring on the same premises, or in the same family, about the same time. All such cases, in addition to the deep so-called bilious color and the red urine, had jactitation, suspirious breathing, inordinate thirst, and vomiting of variously shaded and tinted so-called bilious matters. By diligently inquiring I have ascertained that very many old physicians, some of whom have now retired from practice, are satisfied that they have observed similar cases, sometimes singly and sometimes in groups.
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> The late lamented Dr. A. G. Mabry, in a report of a case of intermitting icterode hæmaturic fever, made to this association in 1870, says: It is a mistake to suppose that this is a new form of disease. More than twenty-five years ago I treated, in the vicinity of Selma, cases of intermitting fever presenting, in a marked degree, all the symptoms characteristic of these cases at the present day.[1]

Although not a new disease in this country, hemorrhagic malarial fever attracted but little attention before the civil war, and probably was frequently confounded with yellow fever, which was by many believed to be an endemic disease in our Southern seaport cities, and which frequently extended from them to smaller towns and country villages, where it was also looked upon as of local origin and not infrequently supposed to be due to malaria. But since the war yellow fever has been generally recognized as an exotic disease, which does not appear in our country unless introduced from abroad, and our endemic hemorrhagic (melanuric) malarial fever has been differentiated from it by the careful studies of numerous physicians in the Southern States.

The increased prevalence of this disease since the war is generally admitted. This is probably due partly to the renewed cultivation of a rich malaria-producing soil in regions where agriculture had for several years been necessarily to a great extent neglected. But it is chiefly, we believe, to be ascribed to the reduced resisting power and greater exposure of the white population, who in the midst of privations were to a considerable extent obliged themselves to perform the agricultural labors which had previously been allotted to their negro servants. This is the answer we would give to the question which Dr. McDaniel presents in the following forcible language:

> And why are some places, once so salubrious that they knew no malarial fevers at all, or if any only the mildest intermittents, then popularly regarded as trivial and almost

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[1] Dr. E. D. McDaniel: Hemorrhagic Malarial Fever, in Trans. Alabama Med. Ass., 1874.

> harmless, now not exempt from even this, the direst of all malarial ills—the very summation of all extreme malarial manifestations? Has not the old malaria acquired a greater intensity? or appeared in more overpowering quantity? or diffused itself to wider limits? or, if a chemical thing, undergone some allotropic change, thus becoming a modified cause and leading to correspondingly modified effects? or has a new malaria sprung into play, acquired the ascendency over the old, and thus brought into prominence the new order of symptoms? or has some new morbific agent allied itself with the old malaria and lent to it additional weapons, fresh power, and greater formidableness? or have the constitution and blood of our people, overpowered in war, bowed down in political despondency, unprosperous in industrial enterprises, stripped of old, accustomed, opulent surroundings, deprived of a liberally varied and nutritious diet, clad in deficiently protective livery, and forced out to greater hardships, greater labors, and greater exposures, felt an intimate, profound deterioration and become unable to withstand successfully, as once they could and as once they did, the unchanged influences of our same old morbid climatic conditions? (Op. cit.)

The disease under consideration is well known in the West Indies, and a good account of it has been given by Sullivan in his "Endemic Diseases of Tropical Climates," under the heading "The Bilious Fever of the Tropics."

Upon the western coast of Africa, and especially in Senegambia, melanuric malarial fever is an extremely common and fatal disease. We are especially indebted to the medical officers of the French navy for an account of it as it occurs upon the African coast, and above all to Bérenger Féraud, who has given us a résumé of the contributions of his predecessors, in connection with his own extended observations, in his valuable work[1] published in 1874.

We shall have occasion to draw largely upon this important work in our further account of the disease under consideration. And first we record the following conclusions reached by the author as a result of his extended and conscientious studies:

> *The most malarious regions are those most fertile in the production of this affection* (p. 241).
>
> Melanuric bilious fever, which is universally considered as a special manifestation of malarial intoxication, is an endemic disease upon the coast of Africa. *Not only has it no etiological relation with yellow fever, but it has absolutely not been influenced by this disease* (p. 66).

The observations of Féraud correspond with those of physicians in the Southern portions of our own country as to the comparative immunity of the negro race. But this immunity is by no means absolute, and a well-marked case in a mulatto is reported; also a fatal case in a full-blooded negro, which did not come under the author's personal observation, but is extracted from the clinical records of the hospital of Gorée.

The researches of Féraud show that while the disease under consideration is undoubtedly of malarial origin, its special clinical features are to a great extent due to certain accessory or predisposing causes pertaining to the individual, which have not, perhaps, in this country, received the attention to which they are entitled. As this is an important subject, and as the increased prevalence of the disease in our own country since the war is doubtless largely due to increased individual predisposition rather than to increased malarial evolution, we shall quote quite fully from the author named with reference to the influence of this etiological factor in the production of *hemorrhagic* malarial fever.

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[1] De la Fièvre Bilieuse Mélanurique des Pays Chauds, comparée avec la fièvre jaune. Étude clinique faite au Sénégal, par L. J. B. Bérenger Féraud, Médecin en chef de la Marine, etc.

> *Influence of Alimentation.*— . . . It is not impossible that the great difference in the number attacked at Saint-Louis or at Gorée, and those who occupy the military posts, that the marked difference as regards the relative frequency of attacks among officers and soldiers is due in part to the difference in food. In the central regions fresh meat is sufficiently abundant and fresh vegetables are not entirely wanting, so that the diet may be varied in a manner supportable by the organization ; but at the posts the Europeans, being for the most part condemned to eat salted provisions and dried vegetables, deprived of fresh meat and green vegetables, are incontestably very badly nourished. I do not, indeed, believe that this bad nourishment induces melanuric bilious fever in preference to any other form of malarial intoxication. It only serves, in truth, to induce profound anæmia very rapidly, and thus leaves the individual disarmed against malaria, of which the disease under consideration is an extreme manifestation.
>
> *Influence of Dissipation.*—This is very considerable, and I do not hesitate to place it at the head of the secondary causes of this disease. In truth, a careful examination demonstrates that in more than one-half the cases the attack has followed the excessive use of alcholic drinks, a prolonged debauch. I have verified the fact more than twenty times in the forty-five cases which I treated in Gorée. It is well known that drunkenness is unfortunately a very common vice among our soldiers : the garrisons in Senegambia form no exception. On the contrary, placed in a country where ennui consumes an individual at each instant ; where the heat of the atmosphere causes a constant thirst ; where nostalgia comes the more easily, inasmuch as the occupations are very restricted, and that the slightest muscular exertion induces fatigue, they frequently become intoxicated. Another cause pushes our soldiers to alcoholism in Senegal : they live in the midst of a negro population frightfully given to drunkenness . . .
>
> This alcoholism is so common among the individuals attacked with bilious melanuric fever, that the first physicians who made autopsies of individuals who had succumbed to this disease considered as pathognomonic an alteration of the stomach which I have demonstrated many times to be only a lesion pathognomonic of the abuse of alcohol—in a word, alcoholic gastritis.
>
> Alcoholism acts as a predisposing cause in producing anæmia ; but it acts also in another manner, more direct and consequently far more potent. It is known that when injested alcohol passes by the portal vein and causes congestion of the liver. . . . We can easily comprehend how this excitement repeated, in addition to other causes, ends by predisposing the individual to hepatic affections, to which category bilious melanuric fever undoubtedly belongs. If we suppose an individual sufficiently prepared by exposure to malaria, we can easily understand how alcoholism may become a determining cause, and, as I have just said, I have many times had occasion to verify the fact that the direct and immediate cause of an attack was a more or less prolonged intoxication. Nothing is more common in Senegal than to see an individual who has been intoxicated for two days attacked on the third day with the prodromes of this disease.

Féraud recognizes refrigeration and insolation as exciting causes of bilious melanuric fever, and suggests (p. 270) that the attacks which are frequently developed by a change of locality, even when this is from an unhealthy to a more salubrious location, are perhaps in great part due to refrigeration. The depressing effect of mercurial treatment is also recognized as a predisposing cause. Our author says in regard to this :

> I would say that mercurial treatment, whether long continued as in syphilis, or of shorter duration as applied to the treatment of the acute endemic affections of hot countries (dysentery, hepatitis), seems to me to be a notable predisposing cause to bilious hæmaturic fever, and I believe that it will henceforth be necessary to give the greatest attention to this point (p. 258).

The influence of a protracted residence in a malarial region, in connection with climatic influences and the secondary causes heretofore mentioned, in establishing an individual predisposition is shown by the fact that in 185 cases 10 only occurred in individuals who had passed less than a year in the colony, while 28 occurred during the second year of residence and 79 during the third year. The number during subsequent years was 37 for the fourth, 9 for the fifth, and 28 for a longer period than five years. The diminution after the third year was due to the fact that a large majority of the Europeans did not remain in the colony for a longer period than three years, and not to any tolerance acquired by long residence.

Relapses are frequent, and instead of exerting a protective influence, as in yellow fever, one attack of hemorrhagic malarial fever constitutes a predisposition in the individual to be attacked again. Féraud says that out of 31 cases which came under his personal observation in 1871, more than half had previously suffered an attack. The same observation was made in 1872 and in 1873. This corresponds with the experience of our physicians in the South who have had opportunities for observing this disease. Dr. Jerome Cochran, of Mobile, Ala., has recently collected extensive data relating to this disease as it prevails in Alabama. He writes me that

> The disease recurs in the same individual an indefinite number of times in successive seasons, and even two or three times in the same season.
>
> It occurs only in malarial regions; is almost always a sequel of chronic chills; may occur in the latter part of summer, in the fall, and even in the winter, and very rarely attacks the negro.

This is quite in accordance with the conclusions of Féraud, who has studied very carefully the seasonal prevalence of bilious melanuric fever in Senegambia and the meteorological conditions which govern this prevalence. Cases occur throughout the year, but the disease is most common in the autumn and winter, "when the marshes have the greatest and most pernicious activity."

According to Colin, this form of malarial fever, which he describes under the heading *fièvre pernicieuse ictérique* (*hémorrhagic, hématurique, fièvre jaune palustre*), was more common in Rome among the civil population than among the French soldiers, whose residence was of comparatively brief duration. He agrees with other authors in saying that those attacked are for the most part individuals who have suffered frequent attacks of intermittent fever and who have arrived at an advanced degree of cachexia.

The relative frequency of attacks of bilious melanuric fever in the French Possessions on the West Coast of Africa is shown in the following table, which we have constructed from the more extended tabular statement given by Bérenger Féraud on page 288 of his work referred to:

Annual Ratio per Hundred of Mean Strength of Cases of the Various Forms of Malarial Fever occurring in the French Possessions on the West Coast of Africa.

		River Posts.			
	Saint-Louis.	Upper Senegal.	Middle Senegal.	Gold Coast.	Gaboon.
Malarial fever.	80.99	773.98	327.12	696.75	630.00
" melanuric .	0.93	21.31	3.90	37.70	53.05
" pernicious..	3.66	9.30	7.80	13.30	13.30

These figures show the frightful prevalence of fatal forms of malarial fever upon this insalubrious coast, where the only chance for a European to escape from the deadly effects of malaria seems to be to escape from the country before his vital resistance is completely overpowered by repeated attacks of the less fatal forms of malarial disease.

In our own country hemorrhagic malarial fever is comparatively rare, even in the most intensely malarious sections. McDaniel says:

> In some localities the seizures, in any given year, do not reach one per cent. of the inhabitants; while in other places a family of ten may have five cases during one season, or fifty per cent. of seizures. In 1871, in the town of Camden, within the corporate limits there were only four cases in a population of eight hundred; and of these four cases only one proved fatal. This would give the ratio of seizures to population one-half of one per cent., of mortality to seizures twenty-five per cent. Throughout the State of Alabama I am satisfied that the seizures are much less than one-half of one per cent. of the population.

CLINICAL HISTORY.—The prominent and characteristic symptoms of the form of malarial fever under consideration are icterus, developed early in the attack, and melanuria—hæmaturia or hæmoglobinuria. Cases of fever attended with passive hemorrhages from the nares, gums, stomach, or bowels, but in which these pathognomonic symptoms are absent, do not properly come under the present heading; and if truly malarial in their origin belong to the group of cases which we have described under the title "Adynamic Malarial Fever," in which such hemorrhages occasionally occur, although comparatively rare, and in which the adynamic and hemorrhagic symptoms are commonly due to a scorbutic or septic complication. As already stated, this disease finds its victims among the older residents of malarious regions who have become cachectic and broken in health from repeated attacks of intermittent or simple remittent fever, or from the combined influence of malaria, improper food, intemperance, etc. Bérenger Féraud says that in Senegal the newly arrived Europeans enjoy an almost complete immunity, and that the arrival of a fresh detachment of troops from France does not at first add to the number of cases admitted to hospital.

Féraud divides the cases into four categories, which he says correspond with the types of ordinary malarial fever, viz.: First, the intermittent (*légère*); second, the remittent (*de moyenne gravité*); third, the pseudo-continued (*de sérieuse gravité*); fourth, the continued or *sidérante* cases (*d'extrême gravité*). He remarks, however, that the terms *légère* and intermittent and *moyenne* and remittent must not be considered as absolutely synonymous, for sometimes the pyrexia in comparatively mild cases may have a remittent character, and extremely grave cases may be intermittent in type.

Dr. McDaniel also recognizes an intermittent, remittent, and pseudo-continued type, and says of the intermittent cases that the paroxysms of fever and the hæmaturia are quotidian. He has never seen a tertian or a quartan, but has seen the alternate days better and worse, "indicating double tertian."

The hemorrhagic attack is commonly preceded by one or more paroxysms of simple intermittent, which may or may not present indications of the grave symptoms shortly to be developed. According to Féraud, these initial paroxysms are usually more severe than those which the individual has commonly experienced in previous non-hemorrhagic attacks, and the chill is especially well marked and prolonged, while usually, in Senegal, the cold stage is scarcely noticeable in ordinary intermittent attacks occurring in old malarial subjects. The initial paroxysm is also followed by an unusual degree of lassitude and muscular soreness, the tongue is heavily coated, and bilious vomiting may occur. Sometimes the following paroxysm is attended with melanuria, and yellow discoloration of the conjunctivæ may be discovered. Or a second still more severe paroxysm may occur, and it is not until the third, or even later, that the characteristic symptoms are developed. Dr. McDaniel says:

> The hæmaturia generally begins in the cold stage, and this is then often very protracted; but it sometimes appears first in the hot stage. The mere act of voiding the bloody urine is, however, distinct from the hemorrhage, and even when the voiding takes place in the hot stage, the hemorrhage may sometimes date back to the chill. The hemorrhage, however, undoubtedly continues and often increases during the hot stage, and disappears only when free sweating is induced. And here let me call especial attention to the important fact that the sweating stage is always, when unassisted, imperfectly developed in all the cases of all forms of this fever, and the most imperfectly in the most severe. When there is adequate and efficient diaphoresis—forming a proper sweating stage—there is generally a distinct intermission in the hemorrhage, and when there is not the one there is not the other.

The urine prior to the attack is often high-colored and "feverish" for some days and deposits a heavy lateritious sediment upon cooling. During the hæmaturic paroxysm it assumes a color which varies from light red, through the various shades of maroon to so deep a red that it appears almost black. The bloody urine is sometimes passed in considerable quantities as often as every fifteen or twenty minutes. McDaniel says that sometimes as much as a pint may be passed every fifteen minutes; but certainly this could only be for a very brief period. Féraud has commonly seen it vary from 150 to 300 grm. in the course of a paroxysm, and once, a fatal case, he noted the excretion of three litres (5.28 pints) during the first melanuric access. In another, non-fatal, case the amount discharged in twenty-four hours was four litres and a half (nearly eight pints). These quantities are said, however, to be exceptional. The urine is almost always acid when first passed, and is more or less albuminous according to the amount of blood contained in it. The specific gravity is from 1020 to 1040. Occasionally, at the outset of an attack, the urine when passed retains a uniform tint and does not deposit any sediment; but usually it deposits very quickly a muddy sediment, of a grayish tint, which may occupy more space than the supernatant and deeply colored fluid portion. In the remittent type the urine often clears up to some extent during the remission without entirely losing its color; and in the gravest cases when there is a period of complete apyrexia the color disappears. In these cases the quantity secreted is often greatly reduced and complete suppression may occur some hours before death in fatal cases. Féraud has not been able to make out any definite relation between the color of the urine and amount of albumen present, and the severity of the attack. He has seen the urine equally black and equally albuminous in the various grades of the disease. The amount of albumen is sometimes so great that when coagulated by heat or nitric acid it completely fills the test-tube. The sediment often contains tube-casts, and the occasional presence of more or less deformed and decolorized blood-corpuscles has been verified by numerous observers. But they are not always found, and the number does not seem to be in proportion to the depth of color of the urine. Indeed, the accounts of the microscopical examination of this fluid given by various observers indicate that in a majority of the cases they are far from being abundant, and that in many a diligent search fails to reveal their presence. If, therefore, the color is in truth due to an escape of blood from the kidneys, as is generally believed in this country, and as is indicated by the name "hemorrhagic malarial fever," by which this disease is known in our Southern States, then we must admit that the red blood-corpuscles, owing to some chemical peculiarity of the urine or to some change in the corpuscles themselves, occurring prior to their escape from the renal vessels, undergo disintegration in a remarkably short period of time, and that the muddy sediment is made up of granular débris resulting from their disorganization. This is the opinion of Professor Tyson, who says:

> In this form of disease, especially, it often happens that the coloring matter only and the débris of blood-disks are found in the urine, very few and often no entire ones being discernible—in other words, we have a true hæmoglobinuria or hæmatinuria. The urine is of course albuminous. A specimen recently received from North Carolina and analyzed by Professor Wormley contained no corpuscles, but revealed the spectroscopic band characteristic of hæmoglobin.

Féraud has arrived at the conclusion that the presence of blood in the urine is exceptional, and that the melanuria is due to bile-pigments. No doubt these pigments are also present in greater or less amount, but we are not prepared to admit that the characteristic appearance of the urine is due entirely, or even chiefly, to these pigments, as Féraud asserts. His opinion, however, is entitled to the greatest consideration, based as it is upon extended observation and an attempt to settle the question by chemical and microscopical tests. He says:

> The very remarkable color of the urine in melanuric bilious fever has caused the vulgar to believe, and for a long time the doctors also, that the liquid contains a large proportion of blood; and I confess that for my part I have been very much struck with it. At first view, it seemed to me very difficult to believe that the color which I had before my eyes was not due to blood, and even to very pure blood, but my opinion has been modified. Several observers have claimed to have material proof that the color is due to the presence of blood. . . . But besides these affirmations we are able to cite a considerable number of observers who have never been able to discover anything comparable with blood-globules. Under these circumstances it was natural that I should wish to form an opinion based upon direct observation. And in the first place, I examined more than twenty different specimens of melanuric urine by means of the microscope without ever discovering a single blood globule. I aways found an abundance of débris of epithelium and uriniferous tube-casts of two kinds—hyaline and granular—but not in a single instance, notwithstanding long and patient researches, anything which resembled, even remotely, the blood-globules.
>
> Not wishing to trust to my personal observations, I have had numerous examinations made by the medical officers under my orders, several of whom had ample experience in the use of the microscope, but no one among them was more successful than myself.

After giving in detail the chemical researches by which the presence of bile-pigments and biliary acids was determined, Féraud states his conclusions as follows:

> We infer from the results obtained—
>
> 1. That the urine of bilious melanuric fever does not contain a trace of blood, and that the very remarkable color which it presents is due to the presence of a large quantity of biliary matters.
> 2. That the bile-pigments which it contains in great quantity, and which give it a dark color like that of Malaga wine, infusion of coffee, etc., are bilirubin and bilifuchsin, to which we must add the biliary acids.
> 3. That these biliary matters are also found in the blood coming from the liver.

Upon returning to Europe Féraud submitted specimens of melanuric urine to the distinguished French chemist, Bouchardat, who decided that the color was due entirely to bile-pigments, and stated that he had previously analyzed numerous similar specimens with the same result.

Féraud does not doubt the correctness of the observations of those who have reported the presence of blood-globules in melanuric urine, but he considers this an occasional and accidental circumstance. Dr. Joseph Jones, of New Orleans, finds both blood and bile in the urine of "malarial hæmaturia." He says:

> The presence of the albumen in the urine of malarial hæmaturia is attended also with colored blood-corpuscles, excretory cells of the kidneys, and casts of the tubuli uriniferi, impacted oftentimes with colored blood-globules.

In the mild form of intermittent hæmaturia Professor Tyson says that the urine deposits a dark reddish-brown sediment, which is generally copious, but varies with the degree of coloration of the urine. "*This sediment is made up chiefly of red* blood-disks, or the granular débris resulting from their disintegration."

In a very characteristic case of bilious melanuric fever, corresponding perfectly with the cases described by Féraud as coming under his observation on the coast of Africa, Professor Jones gives the following account of the microscopical and chemical characters of the urine:

> Amount of urine passed during twenty-four hours, November 30th, 9 A.M., to December 1st, 9 A.M. (1876), 1,560 cubic centimetres. Up to this observation, commencing November 30th, 9 A.M., the urinary secretion had been almost entirely suspended, and the patient states that during the preceding chill and fever he had passed little or no urine.
>
> Heavy deposit of casts of urinary tubes, excretory cells of kidneys, blood-corpuscles, and urate of ammonia and soda, giving the urine a muddy, brownish-red color. This deposit settled very slowly, and the clear urine then presented a deep brown and greenish-black color. The deposit contained blood, and stained bibulous paper of a red and yellow color; and small coagula of blood were also visible. Chemical analysis revealed the presence of the coloring matter and acids of the bile.[1]

It seems desirable, in view of the conflicting evidence before us, that more extended observations should be made with reference to the cause of the discoloration of the urine in this disease; for while we must admit that the presence of blood has been established in numerous cases, yet it is beyond question that bile-pigments are also present in large quantity, and perhaps more uniformly than blood. The disease is essentially a *bilious* fever, and aside from the presence of blood in the urine has no decided hemorrhagic tendency. Healthy blood in normal urine would not give us a fluid corresponding in chemical and physical characters with the porter-colored—sometimes nearly black—urine of this so-called hemorrhagic malarial fever, and it would be a mistake to suppose that renal hyperæmia and passive hemorrhage is alone sufficient to account for the melanuria. Under these circumstances the name given to the disease by Féraud—*fièvre bilieuse mélanurique*—seems more appropriate than that which has been generally adopted in this country—hemorrhagic malarial fever. We have not, however, felt justified in rejecting the latter name, although we are not entirely satisfied that the presence of blood in the urine is the prime cause of the melanuria. Evidently if the discoloration is due to an *excretion* of blood-pigment together with bile-pigments resulting from the destruction of red corpuscles while still in the blood-vessels, the term hemorrhagic is not properly applied to this disease.

Icterus is developed simultaneously with the appearance of melanuria; and so closely are these two pathognomonic symptoms associated that we are justified in believing that both depend upon the same pathological condition. According to Professor Tyson, this is due "not to retention of bile, but to the disintegration of blood-corpuscles and the solution of their coloring matter, which diffuses through the tissues and stains them yellow or yellowish-green. Féraud, on the other hand, believes the yellow discoloration of the skin and tissues to be due entirely to the presence of bile in the blood; and this view is sustained by the observations of Jones, who says with reference to the case previously referred to: "Chemical analysis revealed the presence in the serum of the blood, of the coloring matters and acids of the bile. The deep golden hue of the serum was caused by the bile-pigment, which imparted the golden hue to the skin and conjunctivæ."[1]

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[1] New Orleans Med. & Surg. Journal, Feb., 1878, p. 580.

Icterus is usually first observed at the outset of the paroxysm in which melanuria first appears; but in exceptional cases is developed during the preceding paroxysm. The yellow tint is first noticed in the conjunctivæ and rapidly becomes generalized, so that it is not rare to see a patient who was pale and anæmic before a melanuric paroxysm, in the intermittent form of the disease, present a decided saffron tint at its termination. The discoloration may vary from a slight icteric tint to a deep bronze color. *It is most intense during the febrile paroxysm, at the very time when the urine is deeply colored, and fades out to some extent during the intermission, when the urine has resumed its normal appearance.* This certainly seems to be a very decided indication that the discoloration of the tissues and of the urine is due to the same pathological condition.

"The lips, nails, and all the tissues exhibit the yellow stain; and the discharges from the stomach and bowels, as well as the saliva and the passive cutaneous transudation, when they touch the clothes and bedding impart to these the same tenacious color" (McDaniel). The serum from a blister also exhibits the characteristic yellow color, and according to Féraud, chemical analysis shows that it contains bile.

When the disease runs a favorable course the icteric tint gradually fades and leaves the patient with a dingy white and extremely anæmic complexion. In cases which are quickly fatal the skin is commonly of a deep orange or lemon color, and upon post-mortem examination the tissues generally are found to present the same tint. When, however, the disease runs a protracted course in consequence of the development of adynamic symptoms, the yellow discoloration of the skin and other tissues is less pronounced, and often has almost disappeared before the fatal termination.

Bilious vomiting, so common in all forms of malarial fever, may be considered a constant symptom in this. Even in the comparatively mild cases copious and freqent vomiting of bilious matter occurs as a rule during the febrile exacerbation.

The vomited material is of various shades of yellow or green. Féraud says that after ingested material has been ejected the patient throws up pure bile, which is of a yellowish-brown color at first, but soon assumes a bright green tint, which is so characteristic that if the physician previously had any doubt as to the nature of the case, this should enable him to establish the diagnosis. "If the patient vomits into a white porcelain bowl, for example, the liquid ejected is perfectly limpid, with perhaps a few islands of nasal or pharyngeal mucus floating upon the surface, and is of a beautiful green color, like that of the liquid seen in the ornamental vases in the druggists' windows in Paris and other large cities." In exceptional cases the fluid ejected is yellowish-green instead of being a pure green. In the grave form of the disease the vomited matter is less limpid and may contain suspended particles, which settle to the bottom of the receptacle, where they present the appearance of chopped spinach, while the supernatant fluid is transparent and of a light green color, as in the milder form. In the intermittent type the vomiting usually ceases with the termination of the paroxysm, although some nausea may remain. The amount of fluid ejected, independently of liquids ingested, is often surprising. Féraud has seen a litre (1.76 pint) of the characteristic bilious fluid vomited within two or three hours in the mild form, and in the remittent type a large basin is frequently filled within a brief period. In the gravest cases the retching and vomiting is almost incessant. These cases are attended with intense thirst, but the poor patient no sooner swallows a mouthful of water than it is rejected with distressing retching and the ejection of more or less of the characteristic green fluid. *Hiccough* also frequently adds to the patient's distress, and is not only an extremely intractable symptom but one of grave import.

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[1] Loc. cit., p. 578.

Féraud does not admit that the matter vomited is ever black, unless made so by the ingestion of something which causes it to change color, as, for example, red wine, which gives to the liquid a brownish or almost black color. There should, however, be no difficulty in distinguishing this from the "black vomit" of yellow fever. The following chemical characters are given by Féraud in support of his statement that the green color is due to the presence of biliverdin:

> The substance deposited by the fluid vomited is green and resembles chopped spinach; this substance treated with alcohol gives an emerald-green solution. Nitric acid added in small quantities causes it to change to blue and then to a deep red. Part of this matter is dissolved in a solution of soda and gives a brownish liquid, which when treated with muriatic acid resembles exactly that deposited from the fluid vomited. The same alkaline solution treated with acetic acid gives also an emerald-green color but no precipitate. It is then biliverdin.

The patient, as in other forms of malarial fever, suffers more or less pain in the head and loins, and there is a feeling of discomfort or of absolute pain in the epigastrium and in the right hypochondriac region. This is increased by pressure. By percussion over *the liver* it will be found that its dimensions are very considerably enlarged.

In the severe form of the disease the *headache* is intense and contusive, and the patient often feels as if a cap of lead covered his head as far as the eyes. The expression of the face is indicative of profound depression, and questions are often answered in a hesitating manner, owing to the extreme feeling of fatigue, mental and physical. The respiration is sighing and oppressed; the decubitus is commonly dorsal, and there is less jactitation than in ordinary "bilious fever" and in yellow fever. *The tongue* is broad, moist, not red at the tip and edges, and is covered with a heavy white coating, which becomes yellow when icterus is developed" (Féraud). "In fatal cases it becomes dry and covered with black sordes" (McDaniel).

In the intermittent form of the disease *the bowels* are commonly confined; but in graver cases there are frequent and copious discharges of a thin fluid which resembles exactly in color and consistence the urine discharged at the same time. Féraud says: "It has frequently happened to me to mistake the urine for the intestinal discharges and *vice versa.*" McDaniel says: "The dejections are apt to be watery, copious, deeply yellow or intensely green, sometimes almost black, rarely, if ever, bloody." The *perspiration* has by some authors been said to have a yellow color, but Féraud has never observed this, although he has given particular attention to the point.

In the remittent form of the disease, in favorable cases the remissions become more distinct from day to day, the melanuria disappears, and the icteric tint gradually fades; but the patient is left in a condition of extreme anæmia. During the adynamic period which precedes convalescence *epistaxis* occasionally occurs—in about one out of five or six cases (Féraud). It is not a grave symptom, but calls for prompt treatment by the local application of astringents, and the tampon if necessary, as the patient has no blood to spare. Epistaxis may also occur in cases near a fatal termination in which the patient has fallen into a typhoid condition.

The duration of the attack varies greatly in different cases, and is no doubt largely influenced by treatment. Féraud believes that there is a tendency to the disappearance of the melanuria and the bilious phenomena generally after the second or third paroxysm, both in the intermittent and remittent forms of the disease (p. 185), and he has not succeeded in aborting an attack by the free administration of quinine, although he has several times attempted to do so. He says:

> I have several times found myself in the presence of patients who, after one or two paroxysms of quotidian ague, coming between five and six o'clock in the evening, for example, presented a yellow tinge of the complexion, sufficiently marked to indicate the imminence of an attack of bilious melanuric fever. At the visit the following morning they were at the end of the sweating stage—that is to say, at the most favorable moment for treatment. I hastened to give, sometimes two or three grammes (30 to 45 gr.) of quinine in three doses at intervals of an hour; sometimes this large dose, and at the same time an active purgative in order to relieve the liver. Notwithstanding this treatment the fever returned at the usual hour in spite of a considerable evacuation of bile by the intestine, and melanuria and icterus were developed, the disease seeming to be sensibly modified, but not aborted by this vigorous treatment. In some cases, even, no sensible modification of the symptoms has occurred, and the case has progressed to a fatal termination in spite of my efforts (p. 116).

In the intermittent form of the disease Féraud has found the febrile paroxysms attended with melanuria to recur for two, three, or four days, and then, under proper treatment, convalescence is established, and the patient is discharged from hospital in from eleven to thirty-five days. In the remittent type the febrile period lasts from five to seven days, and is followed by a period of adynamia lasting from three to five days, after which convalescence is slowly established; the patient is detained altogether from twenty to sixty days in the hospital. In the grave form—pseudo-continued—the febrile period lasts seven to nine or ten days, and is followed by a prolonged period—five to eight days—of most profound adynamia; the patients who are fortunate enough to recover are detained in hospital from forty-five to sixty-five days.

The fatal cases are divided by Féraud into two categories. In the first death occurs in from five to ten days as a direct result of the febrile attack, and in the second from the fifteenth to the thirtieth day, from failure to rally from the condition of profound debility which results from the melanuric attack proper. In the gravest form—"*sidérante*"—death occurs in from two to five days in spite of the best efforts of the physician. *Relapses* are common and may occur during convalescence, especially on the seventh, fourteenth, or twenty-first day, or at a more remote period.

PROGNOSIS.—The 268 cases which serve as the basis of Féraud's study relating to the gravity of this disease are divided into four categories, corresponding with the four clinical varieties recognized by this author, viz.: 1, intermittent (*légère*); 2, remittent (*moyenne*); 3, pseudo-continued (*grave*); 4, *sidérante*. The relative number of cases and comparative gravity of the different forms is shown by the following table, which we have constructed from the data given (p. 233):

Form.	No. of cases.	No. of deaths	Relative frequency. Per cent.	Actual mortality. Per cent.
1. Intermittent.....	124	..	46.4	..
2. Remittent.......	64	13	23.5	22.7
3. Pseudo-continued	59	32	22.0	54.0
4. Sidérante.......	21	21	7.9	100.0
Total cases......	268	66	....	24.6

It must not be supposed that recovery is the universal rule in cases having an intermittent type at the outset. On the other hand, many of these cases subsequently assume a remittent or continuous type and are classed with the graver clinical varieties, in which the mortality is considerable.

Dr. McDaniel says with reference to the mortality in the State of Alabama: "I am satisfied that the rate of mortality, the State over, ought not, under proper treatment, to be more than fifteen or twenty per cent. of the seizures." By reference to the following table it will be seen that in Senegal it is even less than this when the treatment consists in the administration of quinine in full doses. Féraud has classified the 286 cases of which he has full clinical notes, with reference to the influence of the treatment employed in relation to the prognosis, with the following result. The letters are substituted for the names of the different medical officers (*chefs de service*) who succeeded each other in the hospitals of Saint-Louis and of Gorée, in which the cases referred to were treated.

	Cases.	Deaths.	Per cent.	
A....	71	22	31	Quinine in very small doses, and calomel purgative.
B....	40	8	20	Quinine in moderate doses; calomel in smaller doses.
C....	29	5	17	
D....	11	4	36	Quinine in very small doses; calomel and other purgatives as the basis of treatment.
E....	42	13	31	
F....	30	9	30	
G....	45	5	13	Quinine in large doses.
H....	18	..	..	

MORBID ANATOMY.—In those cases in which death has occurred early—three to fifteen days—the skin presents a uniform tint, which varies from bright yellow to a deep orange color. In more protracted cases, where death has resulted from consecutive adynamia, this icteric tint is not so pronounced and may be scarcely discernible. The dependent portions of the body often present livid discolorations and stains, due to hypostatic subcutaneous ecchymoses, which give a marbled appearance to the back. This is not seen so constantly as in yellow fever, and is commonly absent in emaciated subjects. Féraud has proved that it results entirely from post-mortem pressure, for when the body is placed immediately after death on the side or on the belly these livid discolorations are still seen only upon the inferior and sustaining surfaces. *Rigor mortis* is commonly well marked.

The *mucous membrane* of the natural orifices of the body is intact and there is no bloody discharge from the nares, mouth, or anus, as is so often seen in yellow fever cadavers. There is nothing special to note with reference to the *brain* and *thoracic viscera* except the yellow staining of the tissues generally, including the meninges of the brain, the pleuræ, and the pericardium.

The *stomach* is also stained yellow and usually contains a little fluid similar to that ejected during life. Féraud says: "Note well that we never find anything which resembles, nearly or remotely, the black vomit of yellow fever. There is simply a reflux of bile in the organ and nothing more; while in yellow fever we often meet with veritable interstitial hemorrhages." And, he might have added, the stomach almost invariably contains more or less of the disorganized blood, which mixed with the acid secretions of the organ constitutes the veritable black vomit of yellow fever.

The mucous membrane is sound unless it was diseased prior to the attack. The softening and increased vascularity which is sometimes observed near the pyloris and at the greater cul-de-sac is said by Féraud to be due to pre-existing chronic gastritis resulting from intemperate habits.

The liver is gorged with blood and considerably increased in volume. The normal reddish-brown color is intensified and it presents a "bronzed" appearance, whereas the liver of yellow fever is pale—straw-yellow, color of old leather, or *café au lait*. The organ both superficially and upon section presents a somewhat marbled appearance, due to the fact that the congestion is not uniform. It seems as if the parenchyma of the gland were occupied by numerous little islands of congestion (Féraud). When death has occurred at a late date the localization of the congestion is still more marked; "the hepatic tissue no longer presents a homogeneous aspect and certain portions are manifestly less gorged with blood than others." When a section is made the blood which flows from the hepatic tissues is dark colored and fluid, and is mixed with bile, which gives it a peculiar purple color. The biliary ducts are filled with bile, which may sometimes be seen to escape in yellow drops if a section is made through a portion of the parenchyma where the more abundant flow of blood from the portal vein does not mask it. The gall-bladder is distended with thick, dark-colored bile, which escapes upon pressure, showing that the distention is not due to obstruction, but to hypersecretion (Féraud).

The spleen is augmented in volume—often double or even triple the normal weight—and may be diffluent when death has occurred at an early date. Otherwise it presents the ordinary aspect of an enlarged spleen in malarial subjects, and is more or less indurated.

The *kidneys* are congested, enlarged, and sometimes softened in spots. The color of the parenchyma is a deep brownish-red, with here and there ecchymotic stains of various dimensions; these are especially found in the cortical substance, and in some instances a veritable renal apoplexy, resulting from interstitial rupture and effusion of blood into the parenchyma, may be observed.

The kidneys after death from malarial hæmaturia present a deep red purple congested hue, and their sections, examined under the microscope, exhibit the tubuli uriniferi filled with coagulated blood. In many specimens I have been able to ascertain that the rupture of the capillaries occurred chiefly in the Malpighian corpuscles, and have been able to trace the tubuli uriniferi through their whole extent, as brilliant opaque cylinders filled with coagulated blood.[1]

DIAGNOSIS.—The clinical features of this variety of malarial fever are well marked, and the diagnosis presents no difficulty. It is established when in a malarial subject—*i.e.*, one who is cachectic as a result of repeated malarial attacks—fever occurs, periodic or continuous in character, attended with melanuria, icterus, and bilious vomiting. It will be seen that melanuria is the essential and distinctive feature of the disease; for we may have a yellow discoloration of the skin in jaundice or in yellow fever, and bilious vomiting is a common symptom in ordinary remittent fever. The combination of these three symptoms, however, belongs only to the disease under consideration.

As the differential diagnosis between hemorrhagic malarial fever and specific yellow fever is often a matter of the greatest importance, and in view of the mistakes which are frequently made, notwithstanding the perfectly well-marked clinical characters of the two diseases, we believe we shall do our readers a service by translating in full the tabular statement which Bérenger Féraud has drawn up, showing side by side the characteristic features of each. The extended opportunities which this author has enjoyed for studying both diseases in the West Indies and on the coast of Africa give an especial value to this table, which contains a reliable and comprehensive summary of his carefully made clinical observations:

Differential Diagnosis between Bilious Melanuric Fever and Yellow Fever.

Bilious Melanuric Fever.	*Yellow Fever.*
The most potent, and indeed indispensable, predisposing cause is a prolonged residence in hot malarious countries.	Prolonged residence in hot countries, malarious or not, gives a certain immunity, increasing with length of residence.
The disease is always preceded by numerous and frequent attacks of malarial fever; simple at first, then more or less complicated, and taking in general more and more a bilious aspect, and which have, in every case, produced a very notable condition of anæmia.	The disease occurs generally in the midst of perfect health, and may occur in persons who have never had an attack of intermittent fever and who are in a most satisfactory condition of plethora.
Icterus appears at once with the first paroxysm at the outset of the disease. It is always present, and gives to the patient from the commencement and throughout the attack a yellow color, which varies from greenish-yellow (*jaune-vert*) to the most pronounced yellow ochre. It is in all the cases general and of a uniform tint everywhere.	Icterus only appears consecutively toward the third day, and is substituted for a red color of the surface[2] which exists at the outset of the disease. It is sometimes absent when the disease is of mild form or if the recovery is rapid. It is limited sometimes to certain regions or presents notable differences as to intensity in different places upon the same individual.
The course is intermittent or remittent at first, and the pulse, the urine, the vomiting follow very exactly these variations. When the fever ceases there is a period of feebleness and of reparation which in no	The course is continuous at first, and has an inflammatory[3] character during two, three, or four days; a transition then occurs; it is sufficiently marked to have been called *mieux de la mort*. For during

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[1] Dr. Joseph Jones, in N. Orl. M. & S. J., Feb., 1878, p. 590.

[2] Due to capillary congestion.

[3] This word is used by the French physicians to show that the fever is ardent, intense, and not to indicate that it is attended with local inflammation.

way resembles the remission of yellow fever, and which is not separated from the febrile stage in a definite and well-defined manner, as in yellow fever. It appears as if the fever yields reluctantly and seeks to return, when the patient succumbs during the febrile period; if he arrives at the period of adynamia, he dies rather from a profound exhaustion than by the effect of phenomena of decomposition.	six to twenty-four hours[1] one might believe that the disease was at an end, and that the patient had entered on convalescence. The second period is perfectly separated from the first by this transition; it is a period of demolition, so to speak, in which the patient is killed by decomposition, suppuration (?), hemorrhages, etc., etc.
The pulse follows the customary variations of malarial fever during the febrile period of two or three paroxysms which constitutes the first portion of the attack; it does not fall suddenly and absolutely, being in all respects similar to the pulse of intermittent paroxysms. Even when the case is progressing favorably we may observe daily fluctuations which are, so to speak, the vestiges of aborted paroxysms.	The pulse is at the outset full and regular, as in a continued fever, and it remains so until the transition that has been called *mieux de la mort* (stage of calm); at this epoch it falls suddenly and remains soft, compressible, and slow.[2]
The cephalalgia is general and increases during the continuance of the febrile paroxysm—six to eight hours—then diminishes very notably, or disappears entirely until the next paroxysm. The patient feels as if he had on a heavy tightly fitting skull-cap.	The cephalalgia is supra-orbital and very intense at first, but it yields rapidly to the means directed against it,[3] or continues without intermission to the end of the inflammatory period—that is to say, during one or two days.
The countenance is depressed and yellow from the outset, or soon after the invasion. The conjunctivæ are of a yellowish color, and never injected and brilliant as if conjunctivitis were commencing.	The face is florid (*vultueux*) and of a bright mahogany color at the outset, and it is only after several days that the *alæ nasi*, the lips, and the eyelids begin to show a yellow color.[4] The eyes are brilliant, the conjunctivæ injected.
The pains in the body extend like a girdle from the loins to the hypochondria; the hepatic and epigastric regions are sometimes extremely painful and sensitive to pressure. Often, however, these pains and muscular pains in the limbs are trifling, and give rise to discomfort and uneasiness rather than to actual pain.	The lumbar pains, which have been called *coup de barre*, are characteristic by their intensity; they are very violent and do not extend like a girdle. The hepatic and epigastric regions are not tender to the touch. There are usually muscular pains of severe character in the limbs, and especially in the calves of the legs.
The vomited matters are bilious, of a decidedly green color, often resembling water in which spinach has been boiled. Vomiting occurs constantly at the outset of the attack, and is arrested at the termination of a febrile paroxysm, to recur with the following one.	Vomiting is not frequent at the outset; in no case is it bilious in character, nor does it present that intermittence which is observed in bilious melanuric fever.
If the vomiting continues after the first or febrile period, it preserves exactly the same characters. The liquid vomited is very transparent, and of a beautiful emerald-green or olive-green color; it stains the linen deeply of a bright green color.	After the inflammatory period, when vomiting occurs it is at first watery and colorless, then gray, then brown, then containing a matter black as soot, which stains the linen brown or black, and not bright green; the black vomit is absolutely opaque when received in a basin.

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[1] Stage of calm.

[2] This account is not accurate as applied to a majority of the cases, for, as shown by Faget, the pulse gradually diminishes in frequency from the outset of the attack, instead of undergoing a sudden depression as stated by Féraud.

[3] Cold to head, hot mustard foot-baths, etc.

[4] The yellow discoloration may commonly be first detected in the conjunctivæ, owing to the white background afforded by the sclerotica.

There is sometimes a bilious diarrhœa from the outset and during the vomiting; later the bowels may be confined, and it is often necessary to administer gentle cathartics.	There is generally constipation at the outset, and diarrhœa only occurs when the case is protracted; it is not bilious, but on the contrary very fetid—an indication of profound decomposition—and often contains a black material[1] which is entirely unknown in bilious melanuric fever.
The tongue is moist, broad, and covered with a thick white coating, which soon becomes stained of greenish color by the matter vomited. The tongue is not red either at the tip or upon the margins; it remains broad, coated, and moist throughout the attack.	The tongue is white in the centre, where it has a cottony appearance, and is red at the tip and edges; it is not so broad, being rather cylindrical. Later it is dry or bleeding, red and tremulous, as in typhoid affections.
The urine is black from the outset; the patient is always very much impressed by the characteristic color. Micturition is generally abundant and frequent, but the melanuria only lasts during the paroxysm. Later the urine is still deeply colored but is not black; it sometimes contains a little bile at this epoch, never at the outset. It is sometimes scanty, but is not suppressed, unless it be for a few hours before death.	The urine at the outset is pale red, or simply febrile; it is limpid and scanty. When the case progresses unfavorably it becomes thick and opaque and less abundant; finally there is often complete suppression one or two days before death.[2]
The paroxysmal fever of the outset may be arrested by quinine, and never calls for antiphlogistic treatment.	The continuous fever of the first period is not controlled by quinine, and calls often for antiphlogistics (?).
The disease is evidently due to malaria; it follows and is followed by paroxysms of intermittent fever; it is absolutely not transmissible from man to man.	The influence of malaria has not been established. The disease is not necessarily, or even usually, preceded or followed by paroxysms of intermittent fever. The transmission from man to man is sadly and terribly frequent (?).
Relapses are very frequent and more and more likely to occur as the attacks are multiplied.	Second attacks are so rare that many physicians have denied that they ever occur.

On another page (86) Féraud gives us the following comparative statement of the appearance presented by the liver in the two diseases upon post-mortem examination:

Volume.—Almost always augmented in a notable manner.	*Volume.*—Not augmented, sometimes normal, often diminished.
Color.—Deeply colored, the color tending to a deep brown; in the interior a granitic red; tissue gorged with blood, moist.	*Color.*—Exterior pale and interior of a straw color, *café au lait*, orange, or gamboge. The hepatic tissue is friable and dry, and resembles mustard flour, yellow or gray.
Traces of local congestion sufficiently intense, resembling sometimes little apoplexies.	No traces of local congestion.

To this we may add that in yellow fever the liver cells are found upon microscopic examination to have undergone fatty degeneration, and that in hemorrhagic malarial fever the black pigment peculiar to malarial affections is usually found in abundance not only in the liver, but in the spleen and elsewhere.

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[1] Altered blood.

[2] The author might have added that except in the mildest cases the urine is albuminous, while in hemorrhagic malarial fever albumen is only present when the urine contains blood.

TREATMENT.—As the disease under consideration occurs only in intensely malarious regions and in the victims of chronic malarial poisoning, we naturally turn to the great antiperiodic, quinine, as the remedy which is most likely to prove of service in arresting its progress, and as our main reliance for the preservation of the lives of the unfortunate victims of this ultimate manifestation of the malignant potency of malaria. And upon referring to the recorded experience of those who have seen much of the disease, we find that quinine is very generally accorded the foremost place in the treatment of this, as well as of other forms of malarial fever, whether mild or pernicious in character. This is the verdict of Bérenger Féraud and his confrères, who have encountered the disease upon the coast of Africa, and of Sullivan, who has had ample experience in its treatment in the West Indies. But lately it has been claimed by experienced physicians in our own country that quinine is not only unreliable as a remedy in this form of disease, but that it is actually injurious. This statement is based upon the observed fact that hæmaturia is sometimes induced or temporarily increased by the administration of quinine, and upon a comparison of the results of treatment with and without quinine.

We can easily understand that a remedy which is almost entirely excreted by the kidneys may do harm when these organs are already overtaxed by the extra call upon their functional activity due to the presence of bile in the blood as well as of the products of tissue metamorphosis in increased quantity as a result of pyrexia. But if the extra tax upon the excretive power of the kidneys is a disadvantage and perhaps a danger, we have to enquire whether this is not more than compensated by the power of the remedy to neutralize the effects of the pathogenic agent to which the renal hyperæmia, hepatic engorgement and hypersecretion, and the accompanying pyrexia are due. Not only do experienced physicians differ with reference to the propriety of administering quinine in hemorrhagic malarial fever, but the supporters and opponents of this method of treatment have each been able to present statistical evidence in favor of their respective views. Under these circumstances the writer feels that it would be presumptuous for him to attempt to decide this important question, and will content himself with recording the evidence at hand, leaving his readers to decide for themselves what course to pursue if called upon to treat cases of this formidable disease.

We remark first, however, that the statistics furnished by Dr. McDaniel, which we give below, afford ample evidence that recovery may take place without the use of quinine, and that on the other hand the assertion of this author that quinine is "dangerous" is not sustained by the results reported by Féraud, and by Dr. Webb,[1] of Alabama, who administer the remedy in large doses.

That the administration of quinine not infrequently increases the hæmaturia has been noted by several authors and is admitted by Dr. Webb, who is nevertheless a strong advocate of the use of this remedy. He says:

> Quinine will undoubtedly, in a certain number of these cases, increase the hæmaturia, and sometimes even seems to cause it. Seeing this, the timid administrator stops his quinine, and his patient dies, with the quinine under the ban of killing him; whereas with a bolder hand, directed by a proper idea of the true cause of this *symptom* (a disturbance of the vaso-motor system under malarial influences), he would have

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[1] Dr. R. D. Webb: Analyses of Thirty-three Cases of Hemorrhagic Malarial Fever, Medical News, Phila., Sept. 1, 1883.

> unhesitatingly continued it, and his patient might have had a good chance to live. Remove the cause of the disease and the hæmaturia will cease. I have seen quite a number of cases to which this remark applies, some in which the quinine, given at the expiration of the second hebdominal period as a prophylactic measure (a measure familiar to all physicians in malarial regions), caused a return of a decided hæmaturia, without fever. In these cases I have not hesitated to repeat the quinine the next day with the best results.

Féraud also appears to look upon the melanuria as a symptom not calling for special treatment, and recommends massive doses of quinine for the cure of the disease, without referring to the possibility that they may increase the melanuria. This author does not admit that the discoloration of the urine is due to the presence of blood, and apparently considers the presence of pigment a result of the excretion of injurious materials from the blood, rather than as due to passive hemorrhage from the kidneys. This view, which we cannot admit to be entirely correct, may have made him indifferent to the effect of quinine in increasing the hæmaturia ("melanuria"), but if so this indifference seems to be fully justified by the results of his treatment—already given in the table on page 309, and which we reproduce here in consolidated form, in connection with the statistics of Drs. Webb and McDaniel.

Author.	Treatment.	Cases.	Deaths.	Ratio.
				Per cent.
Féraud	Quinine in very small doses; calomel purge	71	22	31
Féraud	Quinine in moderate—*moyenne*—doses; calomel in smaller doses.	69	13	17.4
Féraud	Quinine in very small doses; calomel and other purgatives as base of treatment	83	26	31.3
Féraud	Quinine in large doses	73	5	6.8
Webb[1]	Quinine in full doses	23	2	8.6
McDaniel	Quinine administered (no particulars as to amount)	85	35	41
McDaniel	Without quinine	93	16	18

Upon referring to our table it is evident that the statistical evidence is decidedly in favor of quinine if we exclude Dr. McDaniel's series of 85 cases treated with quinine, in which the mortality was forty-one per cent. Certainly we cannot accept this series as evidence that the administration of quinine increases the mortality in the face of the very favorable results reported by Féraud and by Dr. Webb, unless we have fuller details as to the doses in which it was given and the other measures of treatment adopted. We see from our table that in the two series of cases reported by Féraud, in which quinine was given in very small doses, the mortality was thirty-one per cent., whereas in the series in which it was given in large doses it was reduced to 6.8 per cent. Is it not possible that small doses may irritate the kidneys, just as they sometimes irritate the brain, by a local effect (?), and that larger doses may relieve renal hyperæmia, just as they relieve malarial coma, by acting upon the paralyzed vaso-motor nerves, and producing thus a remedial effect which the smaller doses are inadequate to accomplish? However this may be, it is evident that the accessory treatment is an important consideration, and, as we shall see later, Féraud has arrived at the conclusion that the administration of calomel and purgatives as the basis of treatment increases the mortality. The results reported by this author are so favorable to his method of treatment, when we consider the deadly nature of the malarial fevers of the African coast, that our readers will no doubt be glad to have fuller details as to doses, mode of administration, etc.

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[1] In Dr. Webb's series of 24 cases one was treated without quinine and died. In regard to the two fatal cases treated with quinine the remark is made: "Case No. 1 was some distance in the country. I did not see him until in the second paroxysm, and his stomach was in such condition that I was unable to give him quinine with any degree of success. I do not think he was ever under its influence. At this time I had not resorted to its hypodermic use in these cases. Case No. 9 was of a most malignant type. The stomach would not retain quinine. Delirium developed in the first paroxysm, and the patient died comatose, without reaction, from the second paroxysm. Case No. 24, a medical friend, was impressed with the idea that quinine was not required in these cases. At his request, and under protest, I treated him without quinine. The treatment was such as indicated by Dr. McDaniel and others who do not like quinine in this disease. The case was not seemingly severe, and lingered for several days. I have ever regretted that I consented, even at his own request, to treat the case without quinine."

Féraud recognizes two therapeutic indications as presenting themselves at the outset, viz.: the treatment of the bilious condition and of the malarial intoxication—"paludism." The orthodox treatment among the French physicians on the coast of Africa includes the administration of an emetic for the purpose of getting rid of the bile. Féraud himself frequently prescribes twenty grains of powdered ipecac, which assisted with draughts of warm water produces copious bilious vomiting, and is usually followed by diaphoresis and a notable reduction in the force and frequency of the pulse. When the stomach has become calm again after the operation of this emetic is said to be the favorable moment for commencing the administration of quinine. Our author, however, rather permits than recommends the emetic which his predecessors seem to have considered an essential part of the treatment of these cases and to have given as a matter of routine. He says:

> I am disposed, then, to think that, when the indication is not very urgent, we may often spare our patient the great discomfort of an emetic, always extremely unpleasant, especially when we remember that in melanuric bilious fever there is a great tendency to emesis; so much so that this tendency sometimes amounts to a veritable complication, and it seems to me that it is unwise to add to this disposition of the stomach to nausea unless absolutely necessary.

Purgatives are said to be less fatiguing to the patient, and in moderate doses induce abundant bilious discharges from the intestine. Féraud objects to the saline cathartics, with the exception, perhaps, of the citrate of magnesia, on the ground that they are apt to produce nausea; he usually prescribes jalap, ol. ricini, or a purgative enema (which may contain infusion of senna and sulphate of soda). Castor-oil is, however, the favorite cathartic with Féraud, as with most practitioners in tropical regions. He says that if perfectly fresh and made into an emulsion with sweetened water and tincture of peppermint, "it is not repugnant to the eye or to the taste and is an extremely reliable purgative."

From an extended experience Féraud has arrived at the conclusion that the "bilious state is relieved more effectually by opiates than by evacuants." The *sirop diacode* of the French Codex is the preparation preferred, and this is given in moderate doses, repeated every hour in order to bring the patient under the influence of the remedy without inducing dangerous narcotism. He says:

> I may say that in a large number of cases, more than three hundred perhaps, in which no medication had been employed prior to the admission of the patient to the hospital, I have seen the bilious or saburral state rapidly relieved under the influence of this medication, as well and as quickly, at least, as by emetics and purgatives. The patient prefers this mode of treatment incomparably, as it gives him relief and rest, while the emetic of ipecac produces great discomfort and is often followed by protracted nausea.

It is not claimed that the progress of the disease can be arrested by the use of opiates, or that this treatment is always competent to relieve the gastric disturbance and bilious symptoms; but Féraud remarks that in the first period of bilious melanuric fever, as in other febrile attacks attended with bilious phenomena, opiates have given sufficiently good results to make it worth while for the practitioner to bear them in mind.

The second therapeutic indication is considered far more important, and consists in the administration of quinine in full doses for the purpose of arresting the course of the fever as promptly as possible. Féraud asks the question: *When shall we give quinine?* and answers it as follows:

> We may reply in a word, and to show that any temporization constitutes a danger, *as soon as possible*. That is to say, from the first appearance of a remission of the pulse, as soon as there is a little moisture of the skin, a little gastric quiescence; in a word, upon the decline of the paroxysm. If an emetic has been given, the moment arrives an hour or two after the last attack of vomiting; if opiates have been administered, it will be after the second or third dose—that is to say, an hour and a half or two hours after the commencement of medication. In the hospitals of Senegal it is customary to give quinine in solution, in such form that one tablespoonful represents a gramme of the salt. When this is given alone there are some chances that it may be retained, but the contrary happens too often. Some physicians have advised the addition of five to ten drops of laudanum, to aid the stomach in tolerating the quinine. I prefer to give the *sirop diacode* for the same purpose, and, as I have said, it is after having established a tolerance by the administration of one or two tablespoonfuls of the hypnotic that I first give the quinine.
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> In order to avoid as much as possible the chance that the medicine may be rejected, notwithstanding the previous administration of the opiate, it is often best to give the quinine in powder enveloped in a wafer—*pain azyme*—which makes it easier to swallow. And a good plan is to give each gramme in three or four separate portions, at intervals of twenty minutes to half an hour, keeping an exact account of the rejection or preservation of the divided doses. . . . Notwithstanding this precaution, it frequently happens that the absorption of the quinine is prevented by frequent vomiting; and as I attach—with reason, I believe—the highest importance to the retention of this medicine, I resort in these cases to its administration by enema, employing, if necessary, the anal obturator in order to ensure the perfect retention of the medicine in the rectum.
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> It seems to me worth while to give some details upon this subject, in order to show the method of procedure which I believe to be capable of giving the best results It will generally be necessary, first, to give a large emollient enema of warm water in order to clean out the large intestine. After this has come away, twenty to thirty grains of quinine in one hundred or two hundred grammes of water two and a half to five fluidounces) may be injected into the rectum, directly or through the anal obturator. . . . The enema must contain the quinine in the proportion of one per cent., as a larger amount has too irritating a local effect, and, on the other hand, we wish to avoid distending the intestine. By thus using the anal obturator when necessary, and a large enema of warm water in advance, we may be sure of the perfect absorption of the quinine introduced, and it is not necessary to increase the dose beyond measure.

In regard to the dose, Féraud says that it is necessary to have a free hand—"J'ai toujours eu la main lourde pour le sel fébrifuge au Sénégal;

j'ai souvent eu à m'en féliciter et jamais à m'en plaindre." At the outset he would give, as a rule, from thirty to forty grains, and this dose is commonly followed in three, six, nine, or twelve hours by a second dose of fifteen grains.

I have adopted the rule of holding the patient under the influence of the remedy by administering from three grammes (about 45 gr.) to three grammes and a half during the twenty-four hours so long as the fever lasts—that is to say, for three, five, or even eight days. I have taken care to administer the doses in such a manner as to keep up a constant impression, rather than to give large quantities at one time. I have always been governed by the ringing in the ears with reference to the continuance or discontinuance of the remedy after having given thirty to forty grains; that is to say, when the patient complained only of a moderate buzzing, I have not hesitated to give an additional dose of fifty centigrammes (about 8 gr.), but if the ringing in the ears and deafness was very great, I have discontinued the medicine for six to twelve hours.

Féraud remarks that these doses may appear excessive, but that he has never seen any reason to regret giving them, and the following cases are given as evidence of the efficacy of this method of treatment:

M——, corporal of infantry; aged twenty-seven years; thirty months in colony. Arrived from Dakar August 8th, and presented himself at the hospital the same evening. Says he has had fever every day for five days; that he took fifteen grains of quinine this morning and nevertheless has had two attacks of fever to-day, one commencing at 10 A.M. and terminating at 3 P.M.; the second, which commenced at 5 P.M., still continues at the time of his admission to hospital. At this moment his pulse is frequent, his skin burning, the tongue heavily coated, and he complains of frequent nausea, and says that he passed blood with his urine during the day. He walks and speaks like a drunken man. To have hot *tilleul* (tea made of the blossoms of the linden or lime-tree), 20 gr. of ipecac, and 15 gr. of quinine after the vomiting has ceased.

August 9th.—Complete remission at the morning visit; the urine passed during the night was highly colored (slight melanuria). Bouillon; hot *tilleul*; opiate potion, a tablespoonful every hour (*potion diacode*); sulphate of quinine, 30 gr. in four doses, one every hour; emollient enema. At one o'clock in the afternoon the patient had an intense paroxysm of fever, preceded by a violent chill and soon followed by very abundant bilious vomiting of a pear-green fluid containing green particles like chopped spinach; the icteric tint became pronounced, and the urine resumed its melanuric appearance; four bilious stools, which resembled the urine in color; skin dry and burning; tongue still coated. To have effervescing lemonade; 8 gr. of sulphate of quinine to be given upon first appearance of a remission, and when the vomiting has ceased. 7 P.M.: Remission complete; the patient, a very energetic man, tries to get up takes the quinine, and soon after complains of deafness and of loud ringing in the ears.

August 10th.—At the morning visit the patient is without fever and has had a good night; the noise in his ears has disappeared and his tongue is cleaner. Ipecac; opiate potion; sulphate of quinine, 22 gr. in three doses at intervals of an hour. 3 P.M.: Slight heat of skin and acceleration of pulse; urine limpid; to have 8 gr. of sulphate of quinine in two doses.

August 11th.—The condition of the patient is very satisfactory; the pulse is normal; the tongue has cleaned; the icteric tint, which first appeared during the paroxysm of August 9th, has notably diminished; the urine is limpid; one stool in twenty-four hours; the ringing in the ears has slightly diminished since daybreak. Light diet; wine; gum-water; 22 gr. of quinine in six doses at intervals of an hour.

August 12th and 13th.—Condition still favorable; no return of fever, and all the functions are accomplished in a normal manner; he has appetite and wishes already to leave the hospital. Sulphate of quinine, 12 gr. in three doses, one every hour.

August 14th.—The patient felt perfectly well and no medicine was prescribed for him; the following day he was discharged from hospital perfectly cured.

Remarks.—A consideration of this case demonstrates, I think, the efficacy of quinine. The attack was very characteristic and might have become serious. But under the influence of quinine—4.50 grm in two days; 8 grm. in four days; 9.50 grm. in six days—the fever was arrested in forty-eight hours, and convalescence was sufficiently advanced to permit the patient to leave the hospital in six days and a half from the time of his admission. . . . It may be objected, perhaps, that this case is not entirely decisive, as it was of the mild form—intermittent—and that if we had to deal with a case of the graver form—remittent—the success might not have been so marked. We give below a case which sustains our method of treatment, and this time it is not of the mild form, for the patient was very seriously ill at the time of his admission to hospital.

M——, artillerist; aged twenty-three years; twenty-six months in Senegal; fourth admission for intermittent fever; sober; habitually sick.

This patient presented himself at the hospital of Gorée August 10, 1872. His admission ticket contained the following information: He suffered from intermittent fever especially during a five-months' residence at Rufisque, at the end of the winter of 1871. Had previously been in the hospital at Gorée in the month of June, and since that time had had frequent attacks of fever, not very intense and incompletely treated. He presented himself at the infirmary of Castel August 9th, complaining of having had fever at 10 A.M. for several days in succession. He has a coated tongue, loss of appetite, and nausea. Ipecac, 1.20 grm.; sulphate of quinine, 1 grm. in three doses.

August 10th.—Fever returned at the usual hour, but less intense than the day before. Sulphate of quinine, 1 grm. (15 gr.); laudanum, 30 drops.

August 11th.—At the visit to the infirmary the patient complains that he had a violent chill at nine o'clock last evening, which lasted more than an hour. During this paroxysm he passed urine very abundantly, and of such a dark color that he was frightened by it, and brought some in a bottle to show. He complains of pain in the head and lassitude. His pulse is full and about normal in frequency. The skin is slightly moist without abnormal heat. The urine of the night, a portion of which he had preserved, is deeply colored, as if it contained a considerable quantity of blood. The patient was immediately sent to hospital after having taken 1 grm. (15 gr.) of sulphate of quinine.

Upon his admission he presented a slight icteric tint; pulse 80; skin natural; no vomiting; no pain except in the region of spleen and of liver upon pressure. Bouillon; lemonade; sulphate of quinine, 1.50 grm. (23 gr.); potion of *sirop diacode*, 40 grm., to be taken in doses of a tablespoonful every hour.

At 4 P.M. a new paroxysm seemed imminent; the icteric tint was more marked; the urine abundant, highly colored, appearing nearly black, and containing much sediment. No passage from bowels for twenty-four hours; pulse full and somewhat increased in frequence; skin slightly hot and dry; fever soon declared itself. At 11 P.M. he had 0.75 grm. (about 12 gr.) of sulphate of quinine.

August 12th.—Passed an agitated night without sleep; pulse, 116; temperature, 37.8° (100° F.); skin moist; tongue coated; no passage from bowels in forty-eight hours; cephalalgia considerable; some vomiting and nausea in the morning; the icteric tint has become very intense; vomited matter bilious in character but not abundant; urine passed in twenty-four hours, 4 kilogrm. 500 grm. (about 8 pints); the patient says he passed quite as much the preceding night at the infirmary of Castel. The urine is black, bloody—"*sanglantes*"—foaming, and contains much sediment; density, 1016; upon addition of nitric acid it deposits a considerable quantity of albumen; the microscope demonstrates the presence of fragments of uriniferous tubules. Bouillon; effervescing lemonade; purgative enema; potion of syrup of opium; sulphate of quinine, 2.50 grm. (37 gr.) in five doses, at intervals of an hour. 4 P.M.: The patient has had slight bilious vomiting; pulse, 96; temperature, 37.8°; condition unchanged; no ringing in ears; several stools from purgative enema. Sulphate of quinine, 1 grm.

August 13th.—Has had a better night, without agitation, and has slept; the pulse is good; three stools during the night; urine is less deeply colored and contains less sediment; has passed 2 kilogrm. 500 grm. (about 4 pints) in twenty-four hours; the icteric tint appears to have diminished; the skin has an earthy aspect; no vomiting during the night; the patient, who has not previously been able to retain anything, asks for food. The pains in the region of the spleen and liver have sensibly diminished; the quinine has been well supported and absorbed; very little noise in the ears; slightly deaf. The tongue is cleaning; the belly soft; pulse, 94; temperature, 37.7° (99.8° F.). Bouillon; effervescing lemonade; two soft-boiled eggs; beef-tea; sulphate of quinine, 2 grm. (30 gr.) in doses of 0.25 grm. (4 gr., nearly) every hour. 4 P.M.: Condition still satisfactory; the icteric tint has slightly augmented since morning, but without fever, and the patient feels less exhausted; he retained the eggs and the beef-tea; this evening the bouillon was not tolerated by the stomach; sulphate of quinine, 1 grm. in four doses at intervals of an hour.

August 14th.—Same condition; very pronounced saffron tint. The patient suffered for an hour or two from epigastric distress, caused probably by an egg and some bouillon which he had taken. Urine passed in twenty-four hours 1,800 grm. (about 3

> pints); less deeply colored, and contains less sediment; specific gravity, 1016; pulse, 96; temperature, 37.7° (99.8° F.); two stools in twenty-four hours. To have effervescing lemonade; 3 eggs, soft boiled; prunes, crackers, emollient enema; sulphate of quinine, 1.50 grm. (23 gr.). 4 P.M.: Same condition; he retains well the food and medicine prescribed; pulse, 96; temperature, 37.8° (100° F.); no noise in ears or deafness.
>
> August 15th.—Has had a good nignt; the icterus is sensibly diminishing; four stools from enema; pulse, 84; temperature, 37.6° (99.6° F.). The urine is still deeply colored, having a greenish tint, which seems to indicate the presence of bile; quantity in twenty-four hours, 1,000 grm.; the presence of bile is indicated by the reaction when treated with nitric acid; during the preceding days this had not been observed; three stools during day. 4 P.M.: Same condition; pulse normal; skin good. Bouillon; eggs; wine; sulphate of quinine, 1 grm. (15 gr.).
>
> August 16th.—Same condition; the icteric tint has faded notably; the urine is much less colored, and contains less sediment; quantity in twenty-four hours much diminished (600 grm.); specific gravity, 1016; it no longer contains bile. Quarter diet; half allowance of wine.
>
> August 17th.—Still doing well; urine notably colored, but the color diminishes every day; the quantity is normal. Pulse normal; the appetite is improving; the pains in region of spleen and liver have completely disappeared.
>
> August 18th.—Doing well; same prescription.
>
> August 19th.—Same condition; tongue slightly coated; appetite diminished; no passage for twenty-four hours. Enema of sulphate of soda, 45 grm.
>
> August 20th.—Several discharges from enema.
>
> August 21st.—This morning the patient has a bad taste in his mouth, his tongue is coated, and he has no appetite; convalescence does not seem to follow a favorable course. Bouillon; ipecac, 1.20 grm. (18 gr.); sulphate of quinine, 1 grm. (15 gr.).
>
> August 22d.—Under the influence of the emetic there was a decided improvement in the general condition of the patient, and convalescence continued to progress favorably.
>
> *Remarks.*—Here we see a serious attack which yielded in a manner, quite unexpected, to 11.25 grm. (nearly ʒ iij.) of quinine administered during the first four days after the patient's admission to hospital, and although the case was of the remittent type, in which convalescence is always more or less difficult, he was able to leave the hospital in less than fifteen days from the date of his entry.
>
> What can be said after these two observations relating to the abortive action, so to speak, of quinine in full doses? For my part, the results which I have already obtained in more than thirty cases, and almost with certainty, I may say, when the treatment was commenced in time—since I have had the courage to employ the febrifuge in full doses—and eighteen consecutive cures obtained by my excellent friend Dr. Bourgarel, at Gorée, make me believe that we have in this method of treatment an extremely potent means of jugulating the malady.

It will have been noticed that the administration of mercurials has not constituted any portion of the treatment in these successful cases reported by Féraud, and it is evident that recovery may take place independently of the use of this drug, which many physicians in this country consider so essential in the treatment of this and other forms of malarial fever. We cannot give at length Féraud's reasons for not prescribing mercurials in bilious melanuric fever, but quote the following passage from his work, which shows that his experience and researches have induced him to discard mercury altogether. He says:

> The English introduced the fashion of giving calomel in tropical practice, and the French physicians have followed the example of their neighbors. But the English have recognized, a little late it is true, that calomel is an agent which is always dangerous, often inefficacious, and perhaps never necessary [see Morehead, "Diseases of India" (remittent fever)], and the French physicians remain yet in the ancient therapeutic rut, to the great prejudice of their patients, I believe.
>
> I have given all the care of which I am capable to the study of the question relatting to the administration of calomel in bilious melanuric fever, and after having employed it a sufficient number of times, both as purgative and as alterative, after having studied with care the action of this medicine, both in cases which I have seen treated

> by other physicians of the navy and in the clinical records of cases treated by my predecessors, I have arrived at the conviction that the proto-chloride of mercury is far from having the efficacy which some have supposed; and, indeed, that its employment is attended with serious disadvantages under many circumstances. I have, therefore, arrived at the point of rejecting it entirely in my practice, and I base my opinion as much upon an examination of the facts as upon theory.
>
> In more than thirty cases of bilious melanuric fever, of remittent or pseudo-continued type—*forme moyenne ou grave*—I have abstained entirely from giving calomel, and I can affirm that the remission has occurred at least as quickly and as well, I may even say more quickly and completely, in these cases, as in those in which calomel has been given.

It becomes now our duty to present the other side of the question, and first we note that Féraud himself admits that the melanuric attacks frequently disappear without treatment in two or three days. He says on page 353:

> We know since M. Daullé wrote—and we may remark that the posts in Senegal destitute of medical officers are sufficiently numerous in order that the experiment has been, and still is, very frequently made—we know, I say, that when an individual is attacked with bilious melanuric fever, intermittent or even remittent, and receives no medical care, not even quinine, *the melanuric paroxysms succeed each other to the number of two or three in several days, then disappear of themselves.*

While admitting this, however, Féraud is far from admitting that as large a proportion of the cases will recover independently of treatment as under the use of full doses of quinine. He points out the fact that recovery may take place in pernicious malarial attacks independently of medication, yet no one doubts the power of quinine to save life in these attacks.

On another page (115) Féraud admits the failure of quinine in large doses to prevent a threatened attack. He says:

> I have several times found myself in presence of patients who, after one or two paroxysms of quotidian fever, coming between five and six o'clock in the afternoon, for example, presented a yellow tint sufficiently marked to induce a belief that an attack of bilious melanuric fever was imminent. At the morning visit they were at the end of the sweating stage—that is to say, at the most favorable moment for therapeutics, and I have hastened to give sometimes two or three grammes of sulphate of quinine in three doses, at intervals of an hour; sometimes I gave this large dose and at the same time sought to relieve the liver by an energetic purgative. In spite of this treatment [Dr. McDaniel might suggest, in consequence of it] the fever has returned at the usual hour, notwithstanding a considerable evacuation of bile by the intestine, and the icterus and melanuria have not failed to appear. The disease has not been aborted by this vigorous medication, and has only appeared to me to be sensibly modified, and in certain cases it has not even been appreciably influenced, for I have seen it go through its successive stages and end in death in spite of all my efforts.

We have seen that the author just quoted practically ignores the hæmaturia, disapproves of calomel, and addresses his treatment to the cure of the periodic febrile manifestations and attendant derangements of the digestive functions. Dr. McDaniel, on the other hand, considers the first indication to be "to stay the hemorrhage," and according to him calomel has the first place in the list of remedies for this disease. In regard to quinine he says:

> Now, my professional bretheren, I know that I here step upon awful, solemn, dangerous, and responsible ground; and being, in general, as you all know, an advocate of quinine to an extent that few prudent men can claim to exceed, I take the position that I do here, not without having made the proper, thoughtful, and conscientious

> pause. In Dr. East's experience as I read it to you, and in much more that I did not read to you, just as often as he got his patients into a satisfactory condition and then commenced giving quinine, just so often *he plunged them back into hæmaturia*, with its unnumbered woes and dangers. And often in conversations upon this subject with physicians and others, I have had my attention called to cases in which hæmaturia followed quinine, apparently as effect does cause. And over and over, and over again, have I in my own practice observed the hæmaturia re-established or aggravated after quinine; and on the other hand, have seen the disease, with a very formidable array of symptoms, go handsomely on, without one grain of quinine, to a happy convalescence.[1]

The treatment recommended by Dr. McDaniel consists in the administration of calomel in combination with bicarbonate of soda, or with ipecac, and heat to the surface by means of the hot-air or hot-vapor bath; small bits of ice are given to relieve thirst and vomiting; irritating diuretics, such as turpentine, cantharides, etc., are said to be injurious whether taken internally or applied externally, but demulcents and sweet spirits of nitre, or fluid extract of buchu, are said to be useful. No benefit is to be derived from astringents, such as alum, gallic acid, etc.

The importance attached to the administration of calomel is shown by the following extract from Dr. McDaniel's paper referred to:

> First, take about fifteen grains of calomel and fifteen grains of bicarbonate of soda; mix them well and divide into six equal powders, of which give one dry on the tongue, to be swallowed with a mouthful of cold water; give these powders continuously, one every two hours until the constipation is overcome or the diarrhœa corrected. If any one of the powders is thrown back or believed to be thrown back by vomiting, let no time be lost, but another immediately given, and so on until the vomiting is palliated (and this will generally not be long), and let the insatiable thirst in the meanwhile be indulged with pellets of ice if this can be had.

We must refer our readers to Dr. McDaniel's paper for valuable details with reference to the method of using and the efficacy of external heat, and of cold water, which is used under certain circumstances. With reference to the importance attached to the administration of calomel, we may be permitted to remark that if McDaniel has demonstrated that patients may recover without quinine, Féraud has also demonstrated that they may get well without taking calomel, and his statistics are decidedly more favorable to the quinine treatment than are those presented by McDaniel in favor of his method. But we have statistics from another source in which a considerable number (44) of cases were treated without either quinine or calomel, and in which the report is still more favorable, for the patients *all* got well.

Dr. G. B. Malone,[2] of Arkansas, agrees with Dr. McDaniel as to the possibility of quinine producing hæmaturia. He says:

> I know a little girl that always has an attack when she takes quinine, and not otherwise. While I do not believe that quinine will produce the disease, I think I have often seen it precipitate an attack in those predisposed. . . . I kept a record of one hundred cases treated with calomel and quinine, one or both, in which I lost twelve per cent. . . . Especially do I warn you against the use of calomel, quinine, and turpentine. Of the latter I will say this: I have never seen it used in but one case that did not result in suppression of urine and death. I will now proceed to give what I conceive to be the proper treatment of malarial hæmaturia. The first thing that claims your attention will be to relieve the nausea and vomiting. This you can best accomplish with large draughts of cool water. I mean by cool water, that

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[1] Op. cit., p. 18.

[2] Dr. G. B. Malone: Malarial Hæmaturia, Miss. Valley Med. Monthly, p. 62, 1881.

> fresh from the well or cistern—not ice-water ; I would impress upon you the importance of this measure. It washes out the stomach, preventing the medicines from being enveloped in the thick mucus which accumulates in this viscus. It cools the organ, relieves nausea, and is one of the very best diuretics known. It also lowers the temperature and dilutes the excrementitious substances being eliminated from the system through the overworked kidneys. You need have no fear in giving plenty of water ; it should be repeated in large draughts, a pint or even a quart at a time, as often as vomited, until the stomach is thoroughly cleaned and the nausea relieved. When you have accomplished this your patient will be prepared for the remedy, which is hyposulphite of soda and fluid extract of buchu, which I administer in the following dose : ℞. Hyposulphite of soda, grs. xxx.; aqua, ℥ j.; dissolve and add fld. ext. buchu, ʒ j. This dose should be administered every three hours. If vomited immediately it should be repeated ; but if some time elapse, then only the hyposulphite should be repeated. The patient should be kept quiet, and nothing cold should affect the exterior ; a mere change of position or lifting of the cover will sometimes produce a rigor. . . . Under this plan I have treated forty-four cases, every one of which recovered. I know of twelve or fourteen cases treated in my vicinity, with the same result. I have not heard of a single death where the treatment was strictly employed.

Certainly, so far as statistics go this mode of treatment has the advantage; but we are not prepared to admit that the hyposulphite of soda influenced in any very definite manner the favorable result reported by Dr. Malone, in the absence of a series of cases, for comparison, treated by rest in bed and copious draughts of cold water alone.

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